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The authors behind this issue of Scholarly Review produced an enviable body of work rich in novel perspectives and original research. While Scholarly Review has had the privilege of showcasing a great deal of impressive academic work, this batch of scholars stands out for the breadth and depth of their papers, ranging from computational analysis to philosophy. The complexities of the topics covered by the following articles did nothing to deter the students that wrangled and engaged them. Confronting a cultural, political, and academic landscape propped up by palpable emptiness, the words in these pages carry weight.

Jaymin Ding, Pradyota Phaneesh, and Abhiram Atluri, themselves shining stars, find dark matter to be a significant force in the structuring of galaxies.

Kareem Fareed provides a holistic analysis of the molecular signatures of Alzheimer's, Parkinson's and Huntington's Diseases to uncover the commonalities between them.

Youlin Feng takes us to Oceania, where we can enjoy the calming effects of cool glass of Piper methysticum—while trying our best to avoid the hepatotoxicity.

Caroline Jiang tells the bittersweet story of involuntary belief, advocating for new perspectives on the age-old relationship between choice and control.

Youlan Li explores the relationship between menopause and neurological changes, emphasizing the impact of hormonal fluctuations and providing a foundation for holistic interventions.

Annabelle Mass suggests a need for broader integration of music education into educational curricula as a potent tool for fostering empathetic skills in adolescents.

Andrew Rebello, Neerav Mula, and Vineet Burugu bring us back to the skies, offering a model for obtaining information about Seyfert galaxies by differences other than the ratio of the strengths of their emission lines.

Minna Xu determines whether fear appeal, a type of loss framing, effectively motivates people indirectly affected by climate change to take action.

Andrew Yu gives color to our imaginings of the universe, revealing that irregular shaped galaxies are bluer than spirals, and spirals are bluer than ellipticals.



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Mass-to-Luminosity Ratio and Its Correlation To Dark Matter Distributions Across Different Galaxy Types

By Jaymin Ding, Pradyota Phaneesh, and Abhiram Atluri

Author Bio

Jaymin Ding, Pradyota Phaneesh, and Abhiram Atluri are high schoolers who live in the US. Jaymin, a junior in New York, loves STEM, specifically physics, math, computer science, and astrophysics, and is driven to learn new things. Pradyota, a senior residing in Austin, loves learning about all things science. Abhiram, living in Dallas, loves learning new types of math and computer science. When the three came together to study computational astrophysics at UT Austin, a common interest in researching galaxies and dark matter emerged. Through the High School Research Academy (HSRA) program, the group learned about astrophysics and worked on designing astronomical simulations. Their shared passion for math, science, astronomy, and astrophysics led them to continue their research after the program ended. The group received guidance from Professor Shyamal Mitra from UT Austin.

Abstract

Dark matter is believed to play a pivotal role in the structure and dynamics of galaxies. Unlike ordinary matter, dark matter does not emit light or energy or interact with electromagnetic forces. This study explores dark matter distribution in galaxies and compares various galaxy types. We utilize the Spitzer Photometry & Accurate Rotation Curves database, focusing on latetype and early-type galaxies, including Blue Compact Dwarf, Lenticular, Small Magellanic, Tight Spirals, Loose Spirals, Irregular Spirals, and Elliptical galaxies. Using centripetal acceleration and Newton's Law of Universal Gravitation, we derive a galaxy-mass equation within a certain radius. Luminosity within a given radius is graphed through conversions from the database. Results indicate that the mass-to-luminosity ratio generally increases with radius across all galaxy types, suggesting an intertwined relationship between mass, luminosity, and dark matter distribution. The increasing mass-to-luminosity ratio with radius implies that all galaxies tend to have more mass relative to their luminosity as we move further from the center. This supports the idea that dark matter becomes more prominent in the outer areas of the galaxy, forming a dark matter halo and exerting gravitational forces on visible matter to influence the structure of the galaxy. Our results imply that dark matter is a significant part of galaxies.

Keywords: dark matter, galaxy, distribution, SPARC database, mass, luminosity, mass-toluminosity, dark-matter halo



History of the Field

Dark Matter has been a focal point of attention since its discovery. This short literature review allows us to explore the initial findings of dark matter and its implications for the future. The concept of dark matter can be traced back to the observations of Fritz Zwicky in the 1930s (Andernach & Zwicky, 2017). Zwicky noticed inconsistencies between the calculated and observed mass of galaxy clusters, hypothesizing the existence of invisible matter, which he referred to as "dunkle Materie" or Dark Matter. However, it was not until the 1970s that the concept of dark matter gained significant attention. Vera Rubin and her colleagues conducted studies on the rotation curves of galaxies. Their observations revealed that stars located at the outer regions of galaxies exhibited velocities higher than expected based solely on visible matter (Rubin, 1983). This behavior suggested the presence of additional mass, dark matter, spread throughout the galaxy. This was confirmed by other investigators as well (Challinor, 2004; de Swart et al., 2017).

Dark matter holds a crucial role in our comprehension of the cosmos, accounting for roughly 27 percent of the total mass of the universe. Its gravitational influence also plays a fundamental part in shaping the formation of galaxies, providing the essential framework that governs the construction of large-scale structures (Bradač et al., 2008). The nature and composition of dark matter are still not well understood (Feng, 2010).

Research Question and Importance

The mystery of dark matter has been puzzling scientists for a long time. Ever since the discovery that the outer parts of galaxies were moving at the same speed or faster than the inner parts of galaxies, scientists have been searching for what dark matter could be made of.

Our study aims to find the distribution of dark matter in a galaxy based on the radius and then compare the distributions for spiral, elliptical, lenticular, and irregular galaxies. Our galaxy classifications were defined by Hubble in his 1926 paper Extragalactic Nebulae (Hubble, 1926). We also want to compare the dark matter distributions in field galaxies to those in a cluster.

Our research is different because we want to investigate the dark matter distributions across different types of galaxies. We are using existing data gathered from the SPARC database, which contains data on the rotation curves and photometric profiles of a large number of galaxies, to do our research. Many researchers also use rotational velocity as their primary indicator of dark matter; however, we will be using the mass-to-luminosity (M/L) ratio, something that is noticeably rarer in the field. The use of the M/L ratio provides some advantages: unlike rotational velocity, it does not have to be compared to observed mass; high M/L ratios will indicate high dark matter concentrations due to dark matter having mass but not luminosity. The M/L ratio is also independent of galaxy orientation to the observer. Investigating the distribution of dark matter within galaxies is crucial for understanding the structure of the universe, the formation of galaxies, and the nature of dark matter. While scientists lack a full understanding of dark matter, there is strong evidence supporting its existence. Because of this evidence, further investigation of dark matter, including its distribution, is warranted. Understanding the distribution of dark matter would also provide an understanding of astrophysical processes, such as galaxy formation and evolution, and allow testing of theoretical models, including cosmological models. Dark matter would also offer a stronger grasp on the formation of galactic halos and gravitational lensing within galaxies (Refregier, 2003).

Data Sources

SPARC Database

We are using the Spitzer Photometry & Accurate Rotation Curves (SPARC) database of galaxies (Lelli et al., 2016). We specifically focus on the Basic SPARC Data, which is for Late-Type Galaxies, and the Early-Type Galaxies Data (Lelli et al., 2017) for our analysis. Our sample encompasses various galaxy types, including Blue Compact Dwarf (BCD), Lenticular (S0), Small Magellanic (Im), Tight Spirals (Sa), Loose Spirals (Sc), Irregular Spirals (Sm), and Elliptical (E0-E7). By including galaxies



across different classifications, the goal was to capture a wide range of dark matter distribution patterns. The database includes data on 175 late-type galaxies, such as spirals and irregulars (Starkman et al., 2018). It also includes a limited sample of early-type galaxies, such as ellipticals and lenticulars. Its measurements are from Spitzer photometry at 3.6 μ m (which traces the stellar mass distribution) and high-quality H-I, H- α rotation curves (which trace the gravitational potential to large radii).

Highlighted Galaxies

We have chosen the specific galaxies shown in Figure 1 based on their classification and characteristics in order to capture a diverse range of dark matter distribution patterns.

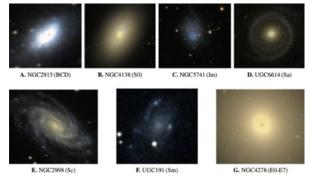


Figure 1. Chosen representative galaxies from the sample population.

Methods

Our first step was to calculate the mass of the galaxies given their rotational velocities. We assumed each galaxy to be circular, simplifying the mathematical modeling and analysis of the data. In reality, different galaxies can vary in shape, so while this assumption is useful, in the future, more complex models may be needed to obtain more accurate data. To gather the data we needed, we followed several steps: downloading, compiling, sorting, and formatting data from the SPARC database, which includes the Basic SPARC Data on Late-Type Galaxies, Early-Type Galaxy Data, Galaxy Samples, Newtonian Mass Models, and Photometric Profiles. We then filter the dataset to 7 specific galaxies of interest, each galaxy representing one galaxy type. We then obtained the rotation curve of each galaxy, found in the Newtonian

Mass Models provided in the SPARC database, and used equation (1) to calculate mass:

$$M = \frac{v_{rot}^2 r}{G}$$

where M is the mass in kilograms contained within the radius r in meters, vrot is the rotational velocity in km/s of the galaxy within that radius, and G is the universal gravitational constant, we can find the mass of the galaxy within that radius. We get Figure 2 with the seven galaxies chosen.

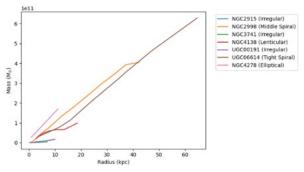
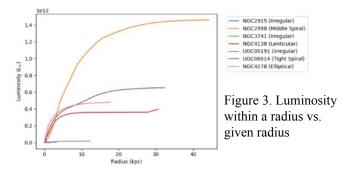


Figure 2. Mass within a Radius vs. Given Radius

As part of the process of finding the dark matter mass distributions, we also found the luminosity of the galaxy to be approximately represented by

$$L = \sum_{i} \left[\left(206265^2 \right) \pi \left(1000R_i \right)^2 \left(10^{0.4(M_{\odot} - S_i - 5)} \right) \right]$$

where L is the luminosity contained within the radius Ri, Si is the surface brightness within the radius, and M is the absolute magnitude of the sun at the measured wavelength, in this case, 3.26 at 3.6 m. Both Ri and Si are measured. In simple terms, the formula works by adding up the amount of brightness (luminosity) of the galaxy at different levels of distance from its center. This summing process is similar to how you would calculate the area under a curve using small rectangles, which is known as a Riemann Sum. Utilizing equation (2), Figure 3 is obtained.





Because the radii were different in the Newtonian Mass Models and Photometric Profiles data, we calculated M/L ratios using the provided Newtonian Mass Model radii to compute mass values and then derived luminosity values through linear interpolation on the luminosity graph (Ding, 2023). We used equations (1) and (2) to calculate and graph the M/L ratio of the galaxy contained within a given radius, shown in Figure 4.

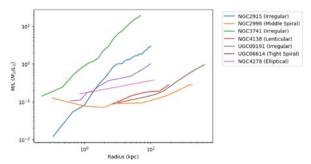


Figure 4. M/L ratio within a radius vs. given radius

Results

In Figure 3, the luminosity curves for all galaxies flatten out at the top, which is to be expected since the stellar density decreases as the radius increases, leading to a decrease in the growth of the overall luminosity. As seen in Figure 4, the M/L ratio starts low for all galaxies and increases.

Initially, the low M/L ratio suggests that there is a smaller amount of mass compared to the luminosity of the galaxies. This suggests that visible matter, such as stars, gas, and dust, and not dark matter, is the dominant contributor to the observed luminosity and that compared to other parts of the galaxy, there is less dark matter in the center.

However, as the radius continues to increase, the M/L ratio begins to rise again. This is likely due to the presence of dark matter. Dark matter is a form of matter that does not emit or interact with light, yet it exerts gravitational effects on the visible matter within galaxies. So, as the radius increases, the gravitational influence of dark matter becomes stronger relative to the luminous matter, causing an increase in the M/L ratio. In other words, the total mass, which includes both visible and dark matter, increases more rapidly than the luminosity alone. As can be seen from Figures 3 and 4, both mass and luminosity increase for any galaxy as the radius in which both are measured increases. It seems that mass has an approximately linear relationship with the radius, while luminosity seems to have an exponential or power relationship with the radius. Interestingly, the M/L ratio, as seen in Figure 4, follows a similar general trend for all the galaxies: it starts low and increases.

A higher M/L ratio represents more mass for a given luminosity. The mass in a galaxy is composed of normal, luminous matter and dark matter. However, only normal matter has luminosity, as dark matter does not give off light or interact with electromagnetic forces. For a given luminosity, a higher mass would mean more dark matter (as dark matter cannot shine), and less mass means less dark matter. Thus, a higher M/L ratio indicates more dark matter. Spikes in the M/L ratio graph could indicate more dark matter at that radius in the galaxy.

Discussion

We chose to compare our research with Sipols, A., & Pavlovich's dark matter research (Sipols & Pavlovich, 2020) due to similarities in the research process, despite the absence of similar papers. Although we did not find publications with methodologies or findings identical to ours, we observed comparable approaches and techniques used in the other study. Additionally, both studies utilized the SPARC database to examine galaxies, facilitating a straightforward comparison of our respective datasets.

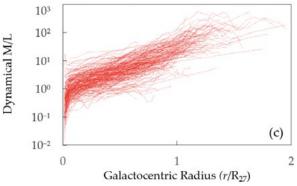


Figure 5. M/L ratio within a radius vs. given radius (Sipols et al., A. 2020)





As we compare Figure 4 and Figure 5, we can see that they both follow a similar trend: the M/L ratio starts low and then rises.

Reflecting on our research, we have made significant progress in understanding the distribution of dark matter in galaxies and its relationship with mass and luminosity. Through the analysis of data from the SPARC database, we were able to examine the M/L ratio within different radii and observe intriguing trends.

One of the most notable findings was the increase in the M/L ratio with radius for all galaxy types. This suggests that as we move further away from the center of a galaxy, the influence of dark matter becomes more prominent relative to the visible matter. This aligns with the concept of dark matter forming a halo around galaxies and exerting gravitational effects on the luminous matter. Comparing our research with Sipols, A., & Pavlovich, we found similarities in the research process and the use of the SPARC database. Although our methodology differed, the overarching results, as well as techniques, were comparable.

One of the main issues that we look forward to fixing and improving upon is our mass calculation. Our mass calculation did not account for velocity dispersion, something which we will add to future research on this topic. Addressing the issue of not accounting for velocity dispersion in our mass calculations is a significant step forward in improving the accuracy and reliability of our research. Moving forward, further investigation is required to delve deeper into the complexities of dark matter distribution and its implications for galaxy formation and evolution. Additionally, exploring the connection between dark matter distributions in field galaxies and those in clusters would provide valuable insights into the influence of the environment on dark matter structures.

Examining the detailed profiles of dark matter halos is also an intriguing area for research. While our research focused on the distribution of dark matter within specific radii, further exploration of density profiles and inner slopes of dark matter halos can provide insights into its properties.

Acknowledgments

We'd like to especially thank the following people: Professor Shyamal Mitra, Ph.D., Professor of Computer Science at the University of Texas at Austin; Professor Karl Gebhardt, Ph.D., Herman and Joan Suit Professor of Astrophysics at the University of Texas at Austin; Álvaro Bernis, María Bernis, and Jose Oñorbe, Ph.D. for developing a cosmology calculator; Dr. James Schombert, Ph.D., Professor of Physics at the University of Oregon; and Dr. Stacy McGaugh, Ph.D., Professor of Astronomy at Case Western Reserve University.

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Emission Line-Independent Method to Classify Seyfert Galaxies

By Andrew Rebello, Vineet Burugu, Neerav Mula

Author Bio

Andrew Rebello is a junior at Staples High School. Andrew has been curious about Astronomy for longer than he can remember -- in fact, he still falls into awe when viewing the night sky. He is interested in pursuing Engineering and Physics as well as conducting more research in the future.

Neerav Mula is a junior at Round Rock High School. Neerav has been fascinated by Astronomy ever since he could read about it. He is also interested in History, Saxophoning, Math, and Computer Science.

Vineet Burugu is a senior at Westwood High School. Vineet loves science. His favorite activity is stargazing through his telescope and viewing faraway planets and galaxies.

Abstract

This study aims to classify Seyfert Type 1 and Seyfert Type 2 galaxies by differences other than the ratio of the strengths of their emission lines, which may allow researchers to discover something new about them that could not be discovered from spectral lines alone. We made use of 43,029 Seyferts from SIMBAD and used Python to analyze 5 properties of each galaxy: spatial distribution, redshift, color-magnitude, morphology, and luminosity. Analysis was done via inspection of graphs and descriptive statistics. Significant differences were found in luminosity, redshift, and color-magnitude. Based on these differences, we trained Decision Tree and Random Forest models to classify a given set of Seyferts as Sy1 and Sy2. The classification was accurate for 76.5% and 78.8% of the testing set for the respective models. Based on our findings, it can be concluded that our model could provide information about Seyfert properties independent of their emission lines.

Keywords: Seyfert Galaxies, Machine Learning, Active Galactic Nuclei, Galaxy Classification, Computational Astrophysics, Astronomy, Emission Lines, Decision Tree, Random Forest

Introduction

Seyfert Galaxies are a particular type of Active Galactic Nuclei(AGN). AGNs are nuclei of galaxies that spew high amounts of energy in the form of electromagnetic radiation. Such galaxies derive their intense activity from the matter of an accretion disk that surrounds a massive black hole. When this matter falls towards the black hole, friction heats it up, causing intense light emissions.

Seyfert Galaxies, discovered in 1943 by Carl K. Seyfert after analyzing NGC 1068 and galaxies with similar properties, have a bright nucleus and wide hydrogen emission lines (Seyfert, 1943). The forbidden lines of Seyferts, on the other hand, are much narrower than the long hydrogen emission lines. In 1967, astronomer Benjamin Markarian created a catalog, the Markarian Catalogue. The galaxies in the Catalogue were selected for their unique ultraviolet emission lines. Naturally, some selections were Seyfert galaxies – about 10%. Although the initial positions of the galaxies in the Catalogue were not initially accurate, they would improve six years later (Weedman, 1977).

Later, in 1974, Khachikian and Weedman created the two main classes used today by Astronomers: Seyfert Type 1 galaxies (Sy1) and Seyfert Type 2 galaxies (Sy2). Sy1 galaxies' Balmer lines can range to around "7500 km/sec in total breadth", making them much broader than their forbidden lines (Seyfert 1943). On the other hand, both the Balmer and forbidden lines are approximately the same width for Sy2 galaxies, with the width of the lines at half-maximum approximately ranging from 500 to 1000 km/s (Chen & Hwang, 2017). Objects with a mix of broad and narrow HI emissionline profiles cannot be classified as entirely Sy1 or Sy2. This led to the work of Osterbrock in 1987: the creation of the Seyfert 1.2, 1.5, 1.8, and 1.9 classifications (Antonucci 1993).

Antonucci theorized a Unified Model for AGN, arguing that the scientific community's classification of different types of AGN results not from intrinsic galactic properties, but from different viewing angles. For instance, Sy1 galaxies may be Seyferts whose galactic plane is viewed face-on whereas Sy2 galaxies are Seyfert galaxies whose plane is viewed edge-on. Antonucci found that NGC 1068, widely considered a Sy2 galaxy by the scientific community, showed broad emission lines, a property typical of Sy1, in polarized spectroscopic observations. His results were strong support for the Unified Model. The shape of an AGN's light emissions is caused by the way gas clouds are distributed or the uneven emission of light. A thick accretion disk or a torus of dust would therefore cause an anisotropic spectrum and explain the difference between Seyfert spectra according to the Unified Model (Antonucci 1993).

Justification of Research Topic

According to a summary of Seyfert research that introduces a paper by Chen, Seyferts have always been classified based on the ratio of the strengths of their emission lines. From Khachikian and Weedman to Osterbrock, classification has always meant looking at the ratio of the strengths of the spectral lines (Chen & Hwang, 2017). Our study proposes to classify based on other properties, which may allow us to potentially discover something new about Seyferts unable to be seen by solely focusing on the spectral lines. The study will also create a unique Seyfert classification model for future astronomers to not only use but also improve.

Sources of Data and Methods

Overview

We searched the SIMBAD database for Seyfert galaxies and found 43,029 Seyferts. We obtained equatorial coordinates, distance, redshift, morphological type, and color-magnitude values for each Seyfert. We solely used the Python programming language and its libraries for data analysis. Queries, data analysis, and graphs can be found on the linked <u>Github</u>.

Morphology

We searched SIMBAD's Seyferts and obtained 2 datasets with different morphological classifications: Hubble Tuning Fork and Hubble Stage T classifications. We used Pandas to clean the data and organize the Seyferts by morphological type. To graph the data, we used MatPlotLib.



Luminosity

Taking the data from SIMBAD, we used Pandas to clean and organize the data, and we used NumPy to format it such that we could graph the data with MathPlotLib.

Color-Magnitude

Two methods were used to analyze color-magnitude: the analysis of statistics and the construction of diagrams. For the raw statistics, we used Pandas to clean, organize, and graph the data into boxplots. For the color-magnitude diagrams, we used Pandas once again for cleaning and organizing the data but converted subsets of the data to NumPy and used MatPlotLib to graph color-magnitude diagrams of the Seyferts in the dataset.

Spatial Distribution

To make an Aitoff Projection of all the Seyferts, we used Pandas to clean the data and MatPlotLib to graph the data. To make a 3-D Model of the Seyferts, we used Pandas to organize and clean the data, Astropy to help compute the X, Y, and Z coordinates in parsecs from Earth, and Plotly to make an interactive 3-D diagram of the data. Using the X, Y, and Z coordinates obtained with Astropy, we used Pandas to procure descriptive statistics and boxplots of the dataset.

Redshift

We solely used Pandas to organize, clean, and graph the data for redshift analysis.

Machine Learning Models

We believed the Decision Tree and Random Forest models were the best models to use because, for our purposes, they were quick to implement among other benefits. Both models tend to be accurate on unseen datasets because they tend to avoid overfitting training sets. Furthermore, Random Forest models benefit from an ensemble of Decision Trees, which, in theory, should lead to better performance. We decided to train both and compare the two as we wanted to see whether more Decision Trees working in comparison would aid classification. Using the three properties in which there was a significant difference, we used Pandas and NumPy to clean the data and split it into training and testing sets, scikit-learn to create the models, and MatPlotLib to graph the Confusion Matrix. Note that for each model, we split the 843 Seyferts into 758 Seyferts for our training set and 85 Seyferts for the testing set – training our models with ~90% of the data and testing it with ~10% of the data. Seyfert type was proportionally represented in the testing and training sets.

Analysis

We analyzed 5 properties of Seyfert galaxies in isolation to determine which of the 5 would pose significant differences.

Morphology

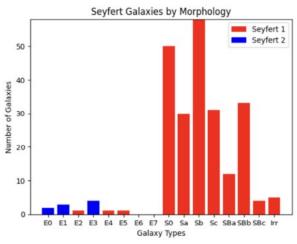


Figure 1. Frequency graph for both Seyfert types by morphology, utilizing already classified galaxies based on the SIMBAD-provided Hubble Tuning Fork classifications.

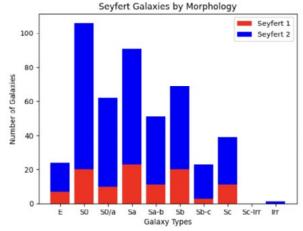


Figure 2. Stacked bar frequency graph for the Seyfert types, using SIMBAD's Hubble Stage T data converted to the Tuning Fork classification.



As seen from the graphs (Figure 1), both sets of data were so imbalanced in terms of morphology across Seyfert Types that we could not draw any significant conclusions about a relationship between Seyferts and morphology based on the SIMBAD dataset alone, causing us to disclude this data from our models.

Luminosity

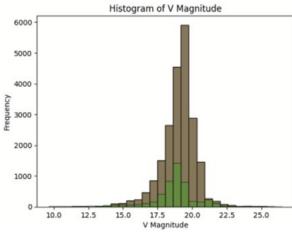


Figure 2. V magnitude histogram for Sy1 and Sy2 Galaxies. Brown bins represent Sy1 data while green bins represent Sy2 data

	8	Mean(µ)	Sid. Dev(6)	Min	QI	Median	Q3	Max	Range
Sy1	21543	19.03	1.21	9.63	18.49	19.19	19.7	26.5	16.87
Sy2	4980	18.73	1.86	6.84	18.2	18.86	19.38	28.34	21.5

Table 1. V magnitude table of descriptive statistics by Seyfert type

Using V magnitudes as a measure of galactic luminosity, we found a significant difference between Sy1 and Sy2 to be the dispersion of magnitudes: the V magnitudes of Sy1 galaxies tend to be much more spread out, which can help the models classify the Seyferts with V magnitudes closer to the extremes (Figure 2). The mean and median of Sy1 V magnitudes are slightly greater than Sy2 V magnitudes (Table 1). These differences make V magnitude a differentiating factor that should be included in our model.

Color-Magnitude

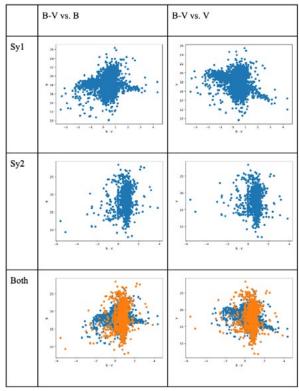


Figure 3. Color-magnitude diagrams of Sy1 and Sy2 galaxies. For the third row, a blue dot indicates a Sy1 galaxy and an orange dot indicates a Sy2 galaxy.

	"	Mean(µ)	Std. Dev(0)	Min	Q1	Median	Ø3	Max	Range			
	Syl Galaxies											
u-g	338	0.57	0.44	-1.52	0.28	0.44	0.78	2.57	4.09			
g-r	338	0.42	0.33	-0.23	0.13	0.43	0.66	2.17	2.4			
гч	338	0.29	0.19	-0.55	0.17	0.32	0.43	0.81	1.37			
i-z	338	0.19	0.21	-1.45	0.07	0.21	0.3	0.81	2.26			
				Sy2 Gala	xies							
u-g	40	1.52	0.39	0.39	1.31	1.53	1.67	2.81	2.42			
g-r	40	0.8	0.19	0.48	0.68	0.79	0.87	1.47	0.99			
ri	40	0.41	0.09	0.18	0.36	0.41	0.44	0.78	0.6			
i-z	40	0.25	0.07	0.04	0.23	0.26	0.3	0.45	0.41			

Table 2. Table of descriptive statistics for Sy1 and Sy2 color-magnitudes.



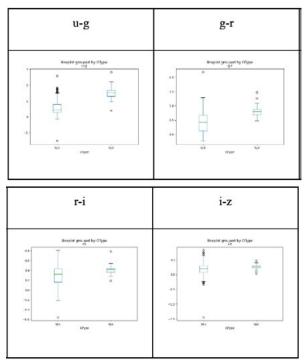


Figure 4. Side-by-side boxplots comparing color-magnitude values by Seyfert type.

V varies more than B for Sy1 but has about the same variation for Sy2 galaxies, so it makes sense when we observe that the B-V values vary more for Sy1 than Sy2 Galaxies (Figure 3). This alone is not yet enough of a difference to include color-magnitude in our model. However, the differences in filter magnitude are significantly greater for Sy2 galaxies (Table 2). This can be further confirmed as one examines the medians of u-g, g-r, r-i, and i-z data: Sy2 galaxies tend to have greater color-magnitude differences than Sy1 galaxies(Figure 4). Therefore, we can include color-magnitude values in our models due to this clear difference.

Spatial Distribution

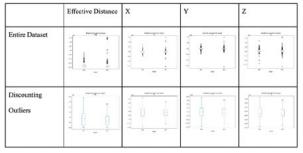


Figure 5: Side-by-side boxplots of Sy1 and Sy2 galaxies for the distance in the X, Y, and Z directions as well as total distance.

	"	Mean(µ)	Std. Dev(σ)	Min	QI	Median	Q3	Max	Range
				s	yl				
Distance	493	10888396 6	114780285	52	22400000	90360000	136500000	850200000	85019 948
x	493	-7565753	105959540	-494035878	-57006810	-11340316	33888544	727273105	12213 8984
Y	493	-4240583	81497518	-444660717	-24427090	-413399	23872136	394510800	83917 517
2	493	22033319	81383224	-566317267	-4085945	9617738	42799914	584348086	12506 5353
			8	s	y2				
Distance	1318	86779947	135999483	182	28750000	61745000	111192500	1773700000	17736 9817
x	1318	-18474862	115104569	-1596736969	-54357696	-17699133	13585283	1488000228	30847 7197
Y	1318	-5381265	89361075	-1595165166	-19219756	-992348	19602502	964135359	25593 0526
z	1318	19278863	63681681	-868548189	-2928979	6905978	36177246	797260688	16658 8878

Table 3. Table of the descriptive statistics of the effective distance, X, Y, and Z positions of Sy1 and Sy2 galaxies.

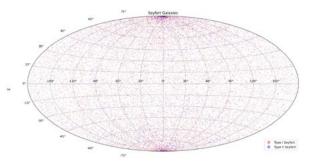


Figure 6. Aitoff projection of all Seyfert galaxies in the SIMBAD database. Red dots indicate Sy1 galaxies and blue dots indicate Sy2 galaxies.

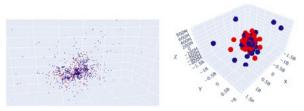


Figure 7. Snapshots of the interactive 3-D plot illustrating the spatial distribution of Sy1 and Sy2 galaxies. Red dots indicate Sy1 galaxies and blue dots indicate Sy2 galaxies.

Based on the boxplots of X, Y, and Z coordinates, there doesn't seem to be a significant difference between the two types of Seyferts concerning their position (Figure 5). The descriptive statistics showed negligible differences between



Sy1 and Sy2 galaxies in terms of position (Table 3). In terms of clustering, Seyfert galaxies do clump in occasional groups of 2s and 3s, but they are not organized into clusters and predominantly tend to be field galaxies scattered throughout space (Figure 6 + Figure 7). Also, including spatial distribution in our models could be a source of error should the models recognize differences that are not representative of reality. Therefore, coordinates and distance will not be included in our model.

Redshift

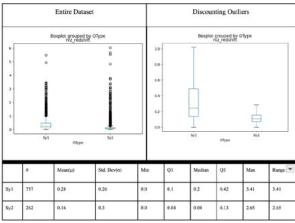


Figure 8. (Top) Side-by-side boxplots of Sy1 and Sy2 galaxies' redshift values. (Bottom)Table that compares the descriptive statistics of Sy1 and Sy2 galaxies' redshift values.

The minimum redshift of both Seyferts was approximately the same(z=0). However, the dispersion, measured via standard deviation and interquartile range, was much higher in Sy1 galaxies than in Sy2 galaxies discounting outliers. If we count outliers, the standard deviations are approximately the same. However, Sy1 galaxies typically have a greater redshift than Sy2 galaxies for both the mean and median of both data (Figure 8). This difference will enable us to include redshift data in our model.

Summary of Analysis

In sum, luminosity, color-magnitude, and redshift are all distinctive properties of Sy1 and Sy2 galaxies that we will use in our models.

Machine Learning Models

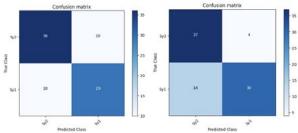


Figure 9. (Left) Confusion Matrix for the Decision Tree model. (Right) Confusion Matrix for the Random Forest model. Note that for both diagrams, numbers in the center of the squares represent the number of Seyferts that had the corresponding true and predicted classes.

We queried SIMBAD for all Seyferts in the database that had data for redshift, luminosity, and color-magnitude. After cleaning the data, 843 Seyferts remained. We used the data to build Decision Tree and Random Forest models, which classified 76.5% and 78.8% of all Seyfert galaxies in the testing set respectively. As the Random Forest was only marginally better, we concluded that both models may serve as equally appropriate classifiers. Furthermore, the results can be more closely analyzed on the Confusion Matrices (Figure 9).

Conclusion

Astronomers have historically classified Seyferts based on emission line ratios: from Carl Seyfert to Khachikian and Weedman to Osterbrock. However, this study has found 3 significant differentiating properties and accordingly created two models that both yielded above 75% accuracy, demonstrating that astronomers can classify Seyferts based on redshift, color-magnitude, and luminosity. In other words, Seyferts can be classified on more than just the strengths of their emission lines. We assume the Unified Model of AGN is false. However, we can still conclude information about the viewing angle and the environment around Seyferts even if the Unified Model is correct. Therefore, this study and the produced models would, whether the Unified Model is correct or not, provide information about a certain Seyfert's properties based on existing information. In terms of sources of error, because we only used SIMBAD, the sample size for our models was small. Therefore, there may not have been enough data for the models to fully realize the true extent to which





Sy1 and Sy2 galaxies differ. Another source of error that stems from using one database is if there was any inherent bias in SIMBAD sampling methods, it would bias our results because we would only be analyzing Seyferts from a certain direction, luminosity, etc. should SIMBAD have such biases.

The models produced in this study as well as stronger models from future work can assist large databases in classifying Seyfert galaxies. The models prove resourceful if such databases cannot provide complete spectral information but instead have complete information about certain properties. In addition, recognizing such a difference could help scientists discover more about this special type of active galaxy.

Comparative Analysis

When we compared our results to other studies in the literature, a study by Chen used a Convolutional Neural Network (CNN), a type of deep learning algorithm, to differentiate Seyfert 1.9 spectra from Seyfert 2 spectra. He obtained 91% precision in classifying Seyfert 1.9 spectra. The cleaned dataset that we used to train the model was composed of 844 Seyferts, while Chen's study consisted of 341 Seyfert 1.9 galaxies and 53,494 Seyfert 2 galaxies. As such, his methods were different: he was able to classify with better accuracy because he had more data and was able to therefore utilize a stronger deep learning model to make better predictions (Chen, 2021). A CNN is superior to a decision tree or random forest, especially with more data, because it independently creates its own categories rather than being assigned categories. In other words, the model may be able to find patterns not initially apparent to human researchers. We used characteristics not often utilized to classify Seyferts (redshift, color-magnitudes, and luminosity). As their differences aren't as stark as emission line strength ratios, it is readily apparent why Chen's model may be more accurate.

Future Work

There is controversy over the morphology of Seyfert galaxies. In terms of future work, our data supports the theory that Sy1 galaxies are typically spiral while Sy2 galaxies are typically elliptical. It would therefore be understandable why Sy2 galaxies vary in luminosity more than Sy1 galaxies: elliptical galaxies vary more in luminosity than spiral galaxies. Furthermore, Sy2 were found to be redder than Sy1 galaxies, corroborating our theory: if Sy1 galaxies are typically spiral, they will be bluer than elliptical Sy2 galaxies. As we were not able to produce experimental results from this theory using SIMBAD data, future work must be done to confirm such conclusions. We may also be able to improve our results if we use a deep learning model coupled with more data from other databases like NED.

Acknowledgments

We would like to thank Dr. Shyamal Mitra for teaching us and supervising the premise of our research – his guidance was vital to our research process. We would also like to thank the Geometry of Space research program at the University of Texas at Austin for providing us with support for our research paper. This research made use of the SIMBAD database, operated at CDS, Strasbourg, France.





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An Analysis of the Relationship between Color and Morphology of Galaxies with Redshift

By Andrew Yu

Author Bio

Andrew Yu is a junior at Plano West Senior High in Plano, Texas. He loves astronomy and anthropography and hopes to study astronomy and astrophysics in college.

Abstract

The research topic derives from my deep curiosity in galaxy evolution. I am asking if there is a correlation between the distance to a galaxy (measured by its redshift) and its color, measured by u-v (ultraviolet magnitude subtracted by visible light magnitude) color index, for galaxies of various morphological types (spirals, ellipticals or irregular shapes). Astronomical data such as redshifts, morphological types, and color indices were queried from the database SIMBAD. Python was used to perform data analysis and to graph data. The best fit function was deployed for polynomial regression with different polynomial degrees to determine the best fitting trend. One-directional trending was not seen throughout, rather, a complex pattern roughly represented by $y = -0.027x^4 + 0.150x^3 + 0.053x^2 - 0.453x + 1.192$ was identified. The downward trend was present only in the redshift ranges z < 1 and z > 3. The study showed that for each morphological type, there is not a simple correlation between a galaxy's distance and its color index. However, a cross-morphological type comparison indicated irregular shaped galaxies are bluer than spirals, and spirals are bluer than ellipticals, which was the case throughout the entire redshift range.

Keywords: SIMBAD, Galaxy classification, Galaxy morphology, redshifts, color index, polynomial regression, python, star formation



Introduction

Galaxy morphology is used by astronomers to categorize galaxies based on their shapes. The most famous classification is called the Hubble sequence, visualized in the Hubble tuning fork, categorizing galaxies into three categories. There are spirals, which have a structure characterized by a disk of spiral arms, which have active star formation regions, and a bright, glowing bulge at the center without the necessary gas and dust to create new stars. Other galaxies, called ellipticals, are less structured: simply an elliptical halo of stars orbiting around a compact center. Ellipticals do not form stars in great quantities. In between the two is a category called lenticular galaxies, which are not purely spiral or elliptical but have similar characteristics to both. Finally, the last category is irregular galaxies, which as the name implies, do not fit in the first three categories. They usually have properties similar to the spiral arms of spiral galaxies, having high star formation rates (Buta et al., 2015).

Many researchers studied the Hubble Sequence with the observations of star formation rates (SFR) based on integrated light measurements in the ultraviolet (UV), far-infrared (FIR), or nebular recombination lines, also simply known as the color of the galaxies (Kennicutt, 1998). Color is important to a galaxy because it can help reveal the populations of stars in the galaxy and the galaxy's star formation rate. High-mass stars are brighter and bluer than low-mass stars, which are red and dim. Luminosity is proportional to mass to the $3\frac{1}{2}$ power (L α M^{7/2}), and since the amount of time a star shines is roughly its mass divided by luminosity, the higher the mass a star is, the shorter the amount of time it will live. Combined with the fact that blue stars are usually brighter than red stars, this means the blueness of a galaxy indicates the galaxy's star formation rate. Established astronomical research has indicated there is a strong correlation between color and galaxy morphology (Smethurst et al., 2021; Gusev et al., 2015). Spiral and irregular galaxies tend to be bluer than elliptical and lenticular galaxies (Skibba et al., 2009), meaning that spirals and irregulars undergo more star formation.

As we examine galaxies at very far distances, we look back into time, effectively allowing a glimpse of the earlier days of the universe through these distant galaxies. Data found on multiple distant galaxies enables us to study their evolution. A form of measuring distance, known as redshift, has become popular. Redshift is the lengthening of light waves due to the motion of the emitting galaxy away from the Earth because of the expansion of the universe, making its light redder than it would appear if it were not moving. It is calculated by dividing the observed wavelength by the known wavelength at certain critical emission lines, and then subtracting 1. For example, if a galaxy's hydrogen-alpha emission lines were observed to be triple the wavelength observed in our own galaxy, the redshift of that galaxy would be equal to 2. At very far distances, which this paper includes, the theory of special relativity must be used to accurately determine the recessional velocity, in the following formula: $z = \sqrt{((1+v/c)/(1-v/c))}$, where v is the velocity that the galaxy is moving away from Earth.

While extensive analysis on galaxy colors at all galaxy morphologies and redshifts have certainly been done, the big picture is still far from complete. For one, little is known about the internal workings of galaxies in the early era of the universe, and what caused such transitions of star formation to form. New discoveries, especially at further redshifts, could be made, allowing a clearer understanding of how our universe today came to be. Though some ideas about the process can be gathered from spectra (Kewley et al., 2019), galaxy evolution remains opaque to the observer.

The research question derives from the author's curiosity in galaxy evolution, asking if there is a correlation between the distance to a galaxy (measured by redshift) and its color for galaxies, and if this varies by morphology.

I asked the question: "Do galaxies become bluer at higher redshifts?", with my hypothesis being that when the distance (redshift) of a galaxy increases, the blue-red color index of the galaxy, adjusted for redshift, will also increase. As the redshift of a galaxy increases, its color index should decrease (becoming bluer), regardless of the morphological type. We expect that after a certain distance from Earth, galaxies of all morphological types will become bluer, because at some point in the past, they needed to be forming stars at a faster rate than now to account for all of the older stars today.



Materials And Methods

For the data in this research project, I used the Set of Identifications, Measurements and Bibliography for Astronomical Data (SIMBAD), a database of extragalactic objects. I chose to use SIMBAD to find the collection of galaxies because it includes data on morphological type, redshift, and color. In addition to SIMBAD, I considered using the Sloan Digital Sky Survey (SDSS), as it is one of the most thorough astronomical surveys conducted, and the NASA/IPAC Extragalactic Database (NED), one of the most accessible to begin addressing my question.

I queried SIMBAD with galaxy measurements of morphology, redshifts, and color index. I used the Hubble morphological scheme for galaxy classification of shape: elliptical, spiral/barred spiral, irregular, and then processed each classification separately. In total, 1603 galaxies were queried from the SIMBAD database and used in the analysis, which is only a tiny fraction of the total number of galaxies in the database, as most did not have the necessary data needed to calculate the u-v color index.

Table 1 displays partial data with header names ID, Galaxy Identifier, galaxy type, redshift, U/B/V color index value and MT (Morphological Type).

#	Galaxy Identifier	type	redshift	Mag U	Mag B	Mag V	MT
1	3C 65	rG	1.176	~	23	~	E D ~
2	Cowie 101	G	1.92	25	24.1525	24.82	I D~
3	NAME SMM J123652+621354	G	1.355	~	22.4	22.3	ID~
4	Cowie 57	G	1.145	23.33	23.4712	24.5	Sc/I: D 2000AJ120. 2190V
5	SHARDS J123656.59+621252.8	G	1.233	~	24.3511	~	Sbc D ~
6	HNM 1215	G	1.84	27.9	26.9	26.4	Scd D \sim
7	[EAD2001] HDFN J123653.43+621221.7	G	1.715	24.64	24.1405	24.67	I D~
8	MODS deep 1627	G	1.24	25.2	25.24	25.22	I D ~
9	TKRS 8664	EmG	1.02	24.35	24.0528	24.24	Sap D 2000AJ120. 2190V
10	GOODS J123648.64+621216.1	rG	1.0662	25.46	26.3837	25.8	Sbc D ~
11	[FLY99] 544	G	1.36	~	~	~	I D ~
12	PEARS n45983	EmG	1.06	23.84	24.0302	25.28	?p D 2000AJ120. 2190V
13	[FLY99] 494	G	1.28	~	~	~	I D ~
14	TKRS 7589	G	1.04	26.4	25.6065	25.53	Scd D ~
15	MODS deep 813	G	1.12	26.5	26.5	26.8	ID~
16	MODS deep 906	G	1.28	26.2	26.4	26.3	I D ~
17	HNM 937	G	1.92	26.3	25.84	26	I D ~
18	Cowie 100	G	1.0188	23.76	23.4996	25.24	I D 2000AJ120. 2190V
19	[CBH2004] 189.166748+62.20214	G	1.0166	25.22	24.7294	24.18	Sbc D ~
20	SHARDS J123639.44+621211.8	EmG	1.18	26.8	26.3572	25.8	Sbc D ~
21	TKRS 7460	G	1.0499	24.07	24.3776	24.73	Sb: D 2000AJ120. 2190V
22	MODS deep 2020	G	1.64	25.7	25.73	25.91	I D ~
23	MODS deep 1481	EmG	1.01	26.9	27	27	I D ~



Spring 2024

Table 1: Raw data (total 1603 galaxies with sufficient u-v index data) from SIMBAD. I filtered the data into galaxies, and then within galaxies, looking for magnitude in near-ultraviolet (300-400 nm) and visible light roughly corresponding to yellow-green (500-600 nm), abbreviated u and v; the measure of redshift, abbreviated as z; and morphological type. SIMBAD collected this data through color filters letting the aforementioned bands of a certain wavelength through. I categorized morphological types into spirals, ellipticals, and irregulars.

The first step was to find the u-v color: this color index measures how much brighter the yellowgreen visible light is than the near ultraviolet light, and has been used to determine "redness" previously, such as in (Zhang and Deng, 2015). This method of color index subtracts the "visible" magnitude from the "ultraviolet" magnitude. For example, a galaxy with "visible" magnitude 14 and "ultraviolet" magnitude 16 would have a u-v color index of 2. Figure 1 shows the rough passbands of the SIMBAD database U and V color filters, the two magnitudes used to calculate u-v color index.

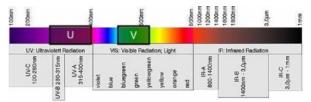


FIGURE 1: The rough passbands of the SIMBAD U and V color filters. Adapted from (Wavelength ranges of electromagnetic radiation)

The second step was to compare the u-v index against the redshift for a given galaxy. As redshift is a function of distance, I used redshift as a stand-in for distance on the x-axis, so in essence, I graphed color by distance. I then broke the data into spiral, elliptical, and irregular galaxies to compare the color by distance relationship for each galaxy type.

I conducted data analysis in Python 3 using Jupyter Notebooks instead of an IDE to run the code, as running chunks of code and visualizing the results right away is only possible with the former. I used the Python library Pandas for my manipulation of the data file and Matplotlib to make my histograms and scatter plots. I also used the NumPy library to handle data analysis. The built-in best fit function in NumPy was used for linear/polynomial regression. Different polynomial degrees were applied to determine the best fit by finding the least square. Matplotlib was used for graphing. All polynomials referenced use my specific x = redshift and y = u-v color index graph axes. Figure 2 shows how a best fit curve is calculated. A polynomial is chosen which minimizes the sum of the squared deviations in the y-direction between the calculated value of the polynomial across all data points.

The solution minimizes the squared error

$$E=\sum_{j=0}^k |p(x_j)-y_j|^2$$

in the equations:

x[0]**n	*	p[0]	+	 +	×[0]	*	p[n-1]	+	p[n]	=	y[0]
x[1]**n	*	p[0]	+	 +	×[1]	*	p[n-1]	+	p[n]	=	y[1]
x[k]**n	*	p[0]	+	 +	x[k]	*	p[n-1]	+	p[n]	=	v[k]

FIGURE 2: Polynomial coefficient calculation

As shown in Figure 3, I first used polynomial regression with degree of 1 for all 1603 galaxies (drawn as dots in the chart) with X axis as redshift and Y axis as U-V index for each galaxy. The red line shows a fit equation y = 0.192x + 1.036. Clearly, a 1st degree linear polynomial does not reveal the correlation between red shift and u-v index. To investigate further, 2nd and 3rd degree polynomials were used to analyze with the same data, and results are shown in Figure 4 and Figure 5. With the increase of polynomial degree, some trends and correlations are shown more clearly.

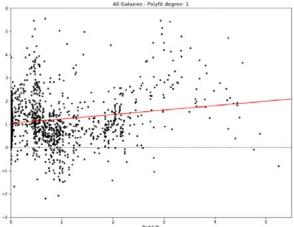


FIGURE 3: Polynomial regression of full galaxy data set with degree 1



Best fit line equation: y = 0.192x + 1.036

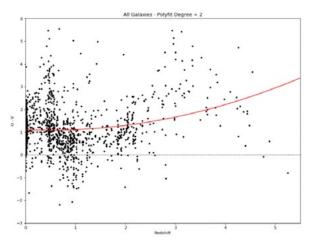
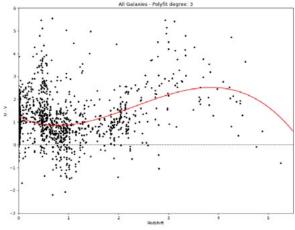
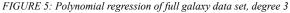


FIGURE 4: Polynomial regression of full galaxy data set, degree 2

Best fit equation: $0.091x^2 - 0.089x + 1.109$





Best fit equation: $-0.114x^3 + 0.798x^2 - 1.043x + 1.235$

Results

The data consisted mostly of low redshift (z < 1) galaxies, however, there were enough galaxies for a useful analysis up until z = 3, with sparse data after that. Figure 6 contains the final results which best reveal the correlations between U-V index, red shift and galaxy morphology types \therefore In this chart, I categorize galaxies with different morphological types with different color and shape. Red triangles represent irregular galaxies, blue stars represent spiral galaxies, and orange dots represent elliptical galaxies. A 4th

degree polynomial was drawn with the best fit function $y = -0.027x^4 + 0.150x^3 + 0.053x^2 - 0.453x + 1.192$, shown as the black line. The same degree was used to draw fit lines for the individual morphological types: a red semi-dashed line for irregular galaxies, a blue dotted line for spiral galaxies, and an orange dashed line for elliptical galaxies.

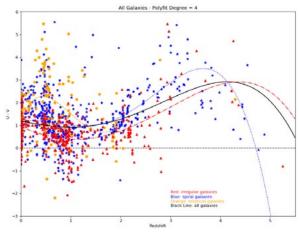


FIGURE 6: Polynomial regression for all galaxies with degree 4, separated by morphological type

I found several interesting yet inconclusive trends in the data.

Between z = 0 and about z = 0.2, there is an upward trend in the u-v value, which shows an increased reddening as galaxies get farther away. Elliptical galaxies also appear to be redder than spirals and ellipticals at this range.

Between z = 0.4 and z = 0.8, there is a vague downward trend in the u-v color index, showing that these galaxies become less red with increasing distance.

Between z = 1 and z = 3, the trend reverses, and u-v color index once again shows a positive trend, so galaxies once again become redder with increasing distance.

After z = 3, the color index appears to trend downwards again, meaning that galaxies this far get bluer with increasing distance. Because of the small number of data points in this range magnifying any inaccuracies, I suspect this is an artifact of the data rather than a true trend.



Discussion

The results are proven not as simple as a downward trending direction as a function of distance. Based on the results, one-directional trending was not seen throughout, rather, a complex pattern roughly represented by $y = -0.027x^4 + 0.150x^3 + 0.053x^2 - 0.453x + 1.192$ was identified.

At low redshift (z < 0.2), the upward trend shows that galaxies do get redder with distance, which is likely due to the effects of redshift itself altering the u-v color index value.

Between z = 0.4 and z = 0.8, the downward trend aligns with my initial hypothesis, but it is not clear why this specific bound has a downward trend and not before or after it.

The upward trend resumes between z = 1 and z = 3, which may again be due to redshift or some other unexplained factor.

After z = 3, if the downward trend is truly valid and not due to a data collection artifact, this may also align with my hypothesis about the early universe having younger and bluer stars.

The study showed that for each morphological type, there is not a simple one directional correlation between a galaxy's distance and its color index. However, cross morphological type comparison indicated irregular shaped galaxies are bluer than spirals, and spirals are bluer than ellipticals.

With several trends present in the data, the hypothesis was proven to be not entirely correct. While I was expecting mostly graphs trending in one direction throughout, the redshifts displayed a complex pattern roughly represented by the polynomial previously given. The downwards trend that I was expecting was present only in the redshift ranges 0.2 < z < 1 and z > 3. This was a trend that held up across all three morphologies, though data for ellipticals were so sparse past z = 2 that accurate conclusions cannot be drawn for them. Interestingly, a similar trend can be seen in the reference papers, so further investigation will be required to confirm reasons for these patterns.

Finally, my initial hypothesis on irregulars being bluer than spirals, and spirals being bluer than ellipticals, turned out to be correct. My findings fit into the conclusion on correlation between color and galaxy morphology by other researchers using similar methods (Smethurst et al., 2021; Gusev et al., 2015). A similar search found spiral and irregular galaxies to be bluer than elliptical and lenticular galaxies (Skibba et al., 2009).

My findings showed a few preliminary relationships, namely the positive trend at z < 0.2 and 1 < z < 3, and the negative correlation at 0.4 < z <0.8, but further investigation is needed to prove these trends. Further research could compare more specific types of galaxies (comparing different types of spirals, ellipticals, or irregular galaxies in addition to lenticular galaxies as opposed to just the three main types) and a broader range of color indices (including blue and infrared filters, in addition to the ultraviolet and visible filters considered here).

Finally, I would welcome a dataset from a different source (such as SDSS or NED) with a greater quantity of galaxies with very high redshifts, as some researchers did on other databases (Smethurst et al., 2021; Zhang and Deng, 2015). The lack of explanation for the findings is not conclusive, and I look forward to continued research.

Conclusion

To answer my question on "Do galaxies become bluer at higher redshifts (as increasing distance from us)", with my hypothesis being that after a certain distance from Earth, galaxies of all morphological types will become bluer, the result shows my hypothesis is not as simple as a downward trend direction. More research can be conducted by analyzing more astronomical data, especially with high redshift galaxies. Furthermore, future research can be expanded using other methods as such:

Use different color indices like u - g or g - v to determine if there are any differences in trends.

Use machine learning libraries like Pytorch to predict properties of galaxies through already identified trends.



Use software to simulate evolution of galaxies themselves and watch if it matches up to the data collected.

Possibly, extend color indices to other areas of the electromagnetic spectrum (gamma rays, X-rays, infrared), which could tell us additional information about galaxy evolution.

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Music Education in the Development of Empathy in Adolescence

By Annabelle Mass

Author Bio

Annabelle Mass is a senior in high school at Harvard-Westlake in Los Angeles, California. With a fervent aspiration to enhance healthcare equality, Annabelle plans to major in Public Health in college. Annabelle's dedication to healthcare accessibility stems from the challenges patients face when self-advocating when there is a language barrier.

Abstract

Empathy, crucial for human relationships, undergoes significant development during adolescence. Empathy versus sympathy is an important distinction because empathy requires someone to feel another person's emotions. This literature review discusses music education for adolescents to develop cognitive empathy. Through the synthesis of studies from trusted databases and academic sources, evidence shows a strong correlation between music education and the development of cognitive empathy, including taking music classes in a group setting and private music lessons. There can be limitations for adolescents to access music education based on economic reasons or if the school offers music education, but music education has many benefits. Music education emerges as a potent tool for fostering empathetic skills in adolescents, suggesting a need for its broader integration into educational curricula.

Introduction

Empathy is a fundamental aspect of human social interaction. The term empathy can be defined as the ability to understand and share the feelings of another (Evans, 2023). As empathy helps hold relationships together, understanding other people's emotions is crucial in relationships. With the importance of empathy in relationships, it is essential to consider how an individual can grow and develop empathy. One of the main components of empathy is cognitive empathy, the understanding of emotions ("Empathy definition: what is empathy," n.d.). Similar to other skills, empathy and the understanding of emotions can be practiced. Also, it is essential to consider how someone's environment influences the skill of empathy. By observing an environment, one can understand different emotions; most of this development of understanding emotions occurs during adolescence. Adolescence is when considerable emotional, cognitive, and social development occurall factors influencing empathy ("Empathy definition: what is empathy," n.d.).

As empathy evolves greatly during adolescence, it is important to consider how adolescents can take advantage of developing this essential skill. Empathy education can be implemented into a curriculum, such as in music classes. Exposure to music classes and music education can increase adolescents' ability to recognize emotions in a group setting and also practice perspective-taking skills. Music education fosters both these skills which are a part of developing cognitive empathy (Rabinowitch et al., 2012; Kiarostami et al., 2022; Wu & Lu, 2021).

Methodology

For this literature review, many scholarly resources were used to compose a comprehensive understanding and deep analysis. This literature review was carried out to select relevant articles from trusted databases such as Google Scholar, PubMed, and JSTOR. When searching through these databases, keywords such as "Empathy," "Empathy Education for Adolescents," "Music Education," "Music Education Developing Empathy," and more terms were used to compile articles. Additionally, articles from universities were used due to the professors' specialties in empathy or music. By harnessing scholarly research, this review aims to gain a robust understanding of the impact of music education on adolescent empathy, enhancing the comprehension of educational policies and their societal responses.

Defining Empathy.

Empathy is fundamentally defined as the capacity to understand and share the feelings or emotions of another person (Evans, 2023). Although the terms "empathy" and "sympathy" are often used interchangeably, the two have distinct meanings (Evans, 2023). Sympathy refers to a feeling of pity or concern for someone's misfortune (Evans, 2023). The distinction between sympathy and empathy lies in the level of emotional involvement: sympathy maintains a level of detachment, representing an understanding of feelings, whereas empathy requires an individual to resonate with and share another person's feelings (Evans, 2023; Brown, 2016). The focus of this paper is on empathy and its role in fostering closer interpersonal relationships through emotional proximity. In contrast, sympathy might inadvertently create emotional distance. Researchers generally categorize empathy into two domains: affective empathy, which entails experiencing sensations and feelings in response to others' emotions, and cognitive empathy, which is the ability to recognize and comprehend others' emotions ("Empathy definition: what is empathy," n.d.).

This paper specifically examines the development of cognitive empathy in adolescents. The skill of cognitive empathy, which is based on recognizing and understanding emotions, is predominantly developed in adolescence ("Empathy definition: what is empathy," n.d.; "The psychology of emotional and cognitive empathy," n.d.). While empathy is partially innate, research indicates that it is a malleable skill, especially cognitive empathy, which can be nurtured over time (Dadds, 2007; "Empathy: A skill you can learn," 2022; "The psychology of emotional and cognitive empathy," n.d.).

Cognitive Empathy Development

While certain individuals may possess a genetic predisposition toward empathy—with evidence suggesting that females often exhibit a



stronger baseline of empathy than males (Toussaint & Webb, 2005)—empathy is notably influenced and shaped by social experiences and interactions (Clarke, 2023). Psychologist Albert Bandura's Social Learning Theory provides a foundational framework for understanding this nurturing process of empathy. Bandura posited that humans absorb knowledge through a synthesis of cognitive and behavioral processes, with environmental interactions being central to this learning process (Bandura, 1977; Bandura, 1985). He delineated observing, modeling, and imitation as primary mechanisms of social learning and further articulated that successful learning through these elements requires attention, retention, skill reproduction, and motivation (Bandura, 1977; Bandura, 1985).

When the Social Learning Theory is applied to empathy, it underscores the vast potential for enhancing empathic capabilities, particularly cognitive empathy. The act of understanding and internalizing another's feelings demands keen observation—a core principle of Bandura's theory (Bandura, 1977; Bandura, 1985; Gerdes et al., 2011). Given that empathy can be cultivated through environmental influences, it becomes imperative to explore how a curriculum can be designed to facilitate empathy development in adolescents(Gerdes et al., 2011).

Developing Empathy Through a Curriculum

Research underscores that empathy, like many other skills, is malleable and can be cultivated over time (Toussaint & Webb, 2005; Ratka, 2018). Like many skills, empathy can be practiced in different ways. However, it is crucial to recognize the influence of an adolescent's personal values and emotional regulation on empathy development (Sike et al., 2018).

The school environment, including extracurricular activities, plays a pivotal role in fostering empathy among adolescents (Sike et al., 2018). As adolescents engage with peers from diverse backgrounds, students are exposed to varied cultures and experiences (Sike et al., 2018). This exposure nurtures awareness and appreciation of differing worldviews, a vital facet of cognitive empathy (Sike et al., 2018). Specific techniques within curricular settings can be employed to bolster empathic skills. For example, enhancing communication has been shown to amplify empathy (Ratka, 2018). Empathy can be taught through role-playing situations because it practices perspective-taking, which is a cornerstone of cognitive empathy (Gerdes et al., 2011). As adolescents practice perspective-taking, they are able to become more aware of other people's emotions and develop cognitive empathy (Gerdes et al., 2011).

The inclusion of art in curricula also presents a potent way to enhance cognitive empathy, particularly in helping adolescents recognize and interpret emotions (Gerdes et al., 2011). In fact, a 2012 study revealed that adolescents who engaged in acting classes exhibited improved empathy(Goldstein & Winner, 2012). The role-playing practices that occur in theater and acting allow adolescents to increase their ability to understand emotions (Goldstein & Winner, 2012).

Beyond the arts, sports serve as platforms for empathy development (Learning to be with others: Using sport to develop empathy, 2022). The team dynamics, interactions, and emotional connections fostered in sporting environments are conducive to understanding and sharing emotions with others(Learning to be with others: Using sport to develop empathy 2022).

Notably, of all activities, music education emerges as a potent instrument in honing cognitive empathy. Numerous studies highlight the nexus between melodic expressions and human emotions, reinforcing the power of music in bridging emotional understanding (Castro & Lima, 2014; Wu & Lu, 2021).

Music Education and Empathy

Music has long been recognized as a powerful medium to express and interpret emotions, and its role in cultivating empathy cannot be overlooked. A critical connection emerges between music and empathy within the intricate networks of the brain, primarily centered in the limbic system, particularly the amygdala (Evans, 2023; Jäncke, 2008; Pour & D'Costa, 2022). This neural overlap underscores the direct link between musical experiences and empathic responses (Kiarostami et al., 2022; Pour & D'Costa, 2022).



As a behavioral intervention, music can foster empathy through social understanding. Music leverages empathy's multifaceted nature—emotional, cognitive, and social—by prompting individuals to relate the musical content to their own thoughts and feelings (Wu & Lu, 2021). Studies have been conducted with adolescents who have received a music education and ones who have not received a music education to test their empathy (Rabinowitch et al., 2012; Kiarostami et al., 2022; Wu & Lu 2021).

For instance, in 2012, Rabinowitch conducted a study of music education in a group setting with adolescents, which showed adolescents who were exposed to group music education were able to significantly improve their empathy scores throughout the study, while this did not occur for the control group (Rabinowitch et al., 2012). Group music education improves adolescents' ability to develop skills for recognizing emotions, which is cognitive empathy (Rabinowitch et al., 2012). Empathy is cultivated through processes akin to those seen in music playing, involving sharing emotions, imitation, synchrony, and collaboration (Rabinowitch et al., 2012; Wu & Lu, 2021). So when adolescents practice music education in a group setting, like in the study, they are able to develop the cognitive empathy skills of understanding emotions through collaboration (Rabinowitch et al., 2012; Wu & Lu, 2021). Such collaborative processes might underscore the development of perspectivetaking, a crucial component of empathy.

Similarly to the 2012 study, in 2022, Kiarostami ran a study with eight different types of music education to test if empathy, including perspective-taking, would develop in adolescents (Kiarostami et al., 2022). Kiarostami's study shows a significant increase in empathy skills for all eight groups of adolescents who had music education (Kiarostami et al., 2022). Also, in the 2022 study, there was a 50% increase in perspective-taking for the music education groups showing that cognitive empathy increased with music education (Kiarostami et al., 2022).

Music can open the doors to adolescence by bringing them together by promoting communication and the recognition of emotions, and the longer exposure an adolescent has to music education, the more they can improve their cognitive empathy by recognizing emotions through music. (Castro & Lima, 2014; Wu & Lu,2021; Kiarostami et al., 2022)

Limitations

Research shows that both group-based music education classes and a variety of music education programs indicated an increase in empathy for adolescents who participate. However, further research is needed to explore the difference between empathy development in group-based music education and individual music education in adolescents. However, the benefits that the two provide should not be overlooked. Music education should be implemented into adolescents' curriculum due to the development of empathy.

Furthermore, the disparity between music education provisions in public versus private schools is noteworthy. Many public schools, constrained by economic challenges, may not provide the same level of access to music education as their private counterparts (Commentary, 2022). This disparity could potentially impact students' scale and nature of empathy development.

Additionally, this paper omits an in-depth exploration of neural pathway development during adolescence due to its complex nature and limited time to perform research for the paper.. Nonetheless, neural pathway development plays a pivotal role in psychological transformations during adolescence, encompassing shifts in identity, self-awareness, and peer evaluations (Blakemore, 2012). These significant changes can influence adolescents' perceptions of emotions—both their own and their peers—which, in turn, can affect their progression in cognitive empathy (Blakemore, 2012).

Conclusion

In conclusion, empathy, a cornerstone of human interaction, plays an indispensable role in forging and maintaining meaningful relationships. The importance of its development during the formative adolescent years cannot be understated. This review underscores the significant interplay between music education and the cultivation of cognitive empathy among adolescents. Music, with its profound emotional resonance and capacity to communicate complex sentiments, emerges as a potent medium for enhancing empathetic understanding. While art



classes, such as acting, offer role-playing opportunities and sports promote group interactions for empathy development, music possesses a unique ability to tap directly into emotional spectra and facilitate nuanced emotional recognition. As demonstrated through the cited studies, group music education not only facilitates the recognition and understanding of emotions but also promotes collaboration, an essential component of cognitive empathy. Additionally, other studies exemplified how music education promotes perspective-taking. It is paramount for educators and policymakers to recognize the potential of music as a tool for fostering empathy. Integrating music education more prominently into curricula could be an investment in nurturing a more empathetic, understanding, and cohesive future generation. As the global community grapples with increasing sociocultural divides, such endeavors in education can act as bridges, harnessing the universal language of music to cultivate empathy.

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The Involuntary Nature of Beliefs

By Caroline Jiang

Author Bio

Caroline Jiang is currently a sophomore at The Bronx High School of Science in the Bronx, New York. She is a writer and a poet with over ten collections of work (one consisting of more than seventy pages), and looks forward to exploring the breadth of her voice. She enjoys spending time with her family and her dog. She also loves delving deep into new things. Currently, she is immersed in the history of Ancient Rome and the complexities of the Classics. She also aspires to explore computer science with interdisciplinary lenses; learn multiple languages; learn Ecclesiastical Latin and Colloquial Latin after completing her current studies of Classical Latin; and read into philosophy.

Abstract

Beliefs are fundamental to an individual's behavior and identity, yet they cannot be picked and chosen by an individual. This paper reviews the role of the individual's voluntary choice and control in the formation of beliefs. It is concluded that the formation of beliefs, consisting of five main stages (Connors & Halligan 2017), is involuntary. Cognitive biases and heuristics and external influences are innate features of the human mind and the nature of beliefs, rendering extensive control over beliefs impossible. Moreover, conscious awareness of involuntary influences is not thorough and does not induce will or control over changing and interfering with the process of belief formation. Though the limitations of the mind and the inability for control seems unfavorable and undesirable, developing an open and adaptive mindset proves to be even more significant. Acknowledging the involuntary nature of beliefs cultivates a perspective that allows for effective examination upon the execution and application of beliefs.

Keywords: Beliefs, Belief Formation, Cognitive Biases, Consciousness, Control, External Environment, Mindset, Heuristics, Volition



Introduction

The desire for control is deeply rooted within human nature. Rather than passive observers, humans are casual agents in their interactions with their environment, and control allows them to optimize rewards and minimize punishments (Leotti et al., 2010). People do not enjoy being, or even the mere prospect of being, held hostage by other influences other than themselves. However, during stressful situations, there is less room for deliberate reflection and controlled response. Instead, an internalized script formed from beliefs is promptly enforced. Given that beliefs dictate how people think and respond in their environment, do individuals themselves have a say in controlling the formation of beliefs? In this paper, I will analyze the process of belief formation, demonstrating how this process is involuntarily shaped by internal factors, such as confirmation bias and the availability heuristic, and external influences, including cultural values and practices. Despite this involuntary nature, an adaptive mindset proves as beneficial for executing individuals' will after the formation of beliefs.

Belief Formation

Beliefs can be considered as propositions that one regards as true or probably true, even without full intellectual knowledge (Seitz & Angel, 2020). Beliefs are fundamental to the reality of individuals, allowing them to develop a personal affective stance and interpretation of their environment (Seitz & Angel, 2020). Beliefs guide behavior and the decision-making process, especially when decisions have to be made instantaneously and in the spur of the moment (Leicester, 2008). Individuals can trust their beliefs at any given time, despite incomplete or possibly unreliable knowledge, to react quickly and accordingly.

The formation of beliefs is an involuntary process. There are five main stages that account for the process of forming beliefs (Connors & Halligan 2017). The first stage is a precursor that shapes the content of a future belief (Connors & Halligan 2017). This involves direct experience or any external influences. The second stage is a search for meaning to account for the precursor (Connors & Halligan 2017). Meaning is found from pre-existing beliefs, emotions

that arise, and the surrounding environment. The third stage is an evaluation of the belief to maintain internal consistency (Connors & Halligan 2017). This evaluation is based on the degree of satisfactory explanation for the precursor, the positive or negative mood of the subject, and the coherence of the belief associated with pre-existing beliefs. The fourth stage is accepting and holding the belief (Connors & Halligan 2017). Beliefs may be held with varying levels of conviction, depending on the evaluation criteria of the third stage. The fifth stage is the consequential effects of holding the belief (Connors & Halligan 2017). The higher level of conviction and the greater the relevancy of this newly formed belief in the environment may result in radical changes in the subject's cognitive processes, reality, behavior, and even memory. Despite this seemingly deliberate process, subjects can still remain unaware that they hold a particular belief. This kind of belief will simply be assumed to be an accurate view of reality, even without the subject's will or conscious choice to do otherwise.

Cognitive Biases

Belief formation suffers from inherent limitations, namely biases. Throughout this process, the mind takes certain mental shortcuts of heuristics, cognitive strategies that allow for quick judgments without deliberation, and biases to reduce cognitive efforts (Tversky & Khaneman, 1974). Cognitive biases, the systematic but flawed patterns of responses in judgment and decision-making (Wilke & Mata, 2012), prove that beliefs are susceptible to involuntary processes beyond an individual's immediate control. I will outline the involuntary nature of several common biases: confirmation bias, anchoring bias, and representativeness heuristic.

Confirmation bias is the tendency to search for information that supports existing beliefs and ignore or distort data contradicting them to create a consistent internal environment (Peters, 2022). Confirmation bias is prominent throughout the process of belief formation, as pre-existing beliefs and perceptions dictate many of the stages involving internal consistency and reasoning of belief. This bias is an innate feature of the mind, independent of intelligence, cognitive ability, or motivation to avoid it (Peters, 2022). For instance, a researcher studying Alzheimer's disease may hold the belief that





memory games improve and delay memory loss. Due to confirmation bias, the researcher actively seeks evidence confirming this belief and interprets results in accordance with this belief, while discounting opposing perspectives. This is not necessarily a reflection of the researcher's competence, intelligence, or motivation to avoid bias, as confirmation bias is often unconscious and unintentional.

Individuals have the tendency to resist change after an initial hypothesis is formed due to anchoring bias (Lehner et al., 2008). Anchoring bias is mainly involved in the later stages of belief formation (stages three and four) as beliefs are evaluated and held. Prior beliefs overpower and shield the impact of subsequent beliefs, thereby hindering the acceptance of new information and new beliefs. Anchoring bias is difficult to control. An individual may unknowingly be affected by this bias, providing no reason to change their beliefs. Without conscious or voluntary will, fallacious and harmful beliefs may be formed and accepted.

Representativeness heuristic is a cognitive strategy for making categorical judgments about someone based on how closely they match a generalization (APA Dictionary of Psychology, n.d.). This heuristic mainly causes individuals to form stereotypes and prejudices. Individuals will tend to make generalizations that guide perceptions without deliberate thought or choice. For instance, individuals with multiple piercings and tattoos are often stigmatized and perceived as less professional. Under the influence of the representativeness heuristic, an employer may perceive a job candidate with such appearances as unsuitable and unprofessional.

Despite limited knowledge or narrow perspectives, new beliefs are formed depending on pre-existing beliefs to maintain internal consistency with the overall belief system (Tversky & Khaneman, 1974). The development of cognitive biases and heuristics is challenging to prevent– it is a builtin responsive system, akin to the "fight or flight" response, serving as an evolutionary and adaptive feature. These biases operate at a subconscious level, shaping beliefs without deliberate volitional control.

External Influences

Similar to how an individual's environment cannot be controlled, the formation of an individual's belief also cannot be controlled. External influences of the social environments cause belief formation to be involuntary. These influences play a role in all five stages of belief formation, and are responsible for forming and reinforcing beliefs. Direct experience encompasses external influences, and is the strongest effect since it provides a natural credulity and an innate tendency to believe (Sathyanarayana Rao et al., 2009). These experiences are acquired through an individual's upbringing and social interactions, independent of choice. The beliefs of significant others surrounding an individual during childhood, such as a parent, can be adopted and can influence one's perception of reality. In a study by Frome and Eccles (1998) investigating the effect of parents' perception on their children's grades and self-perception, it was found that parents are determining factors of how a child perceives reality. Thus, the formation of beliefs are heavily influenced by interference of others in childhood development and in the social environment, mainly those who hold great significance and impact (such as close relationships, with great emotional significance).

Culture provides a shared system of values, beliefs, and practices, affecting people's behavior and their mind (Gao et al., 2022). This shared system affects one's perception and stance on an issue and shapes a person's beliefs through the lenses of a particular group. Herd mentality, "the tendency of the people in a group to think and behave in ways that conform with others in the group rather than as individuals" (Merriam-Webster, n.d.), describes the innate drive to submit to the majority of a society and culture at the expense of individuality. For example, many Chinese smokers have adopted the cultural belief that smoking is a sign of maturity, is stylish, and is socially beneficial, causing them to continue smoking despite the harmful health effects (Ren et al., 2019). This shows how beliefs are guided and reinforced through social and cultural conditioning.



Limitations

The relationship between consciousness and will may be disputed in my argument. It may be pointed out that humans are capable of willful cognitive change. In the preliminary stages of belief formation, sensory inputs from the environment enter an individuals' brain, and beliefs filter out which information should enter conscious awareness (Sathyanarayana Rao et al., 2009). When an individual changes their thinking and becomes more open and receptive, they can access the information filtered out and change their beliefs (Sathyanarayana Rao et al., 2009). Thus, it may be concluded that heuristics and biases in this process can then be reassessed and beliefs can be critically re-examined.

However, conscious awareness of all external stimuli does not guarantee that beliefs will be formed void of interference. It is even not guaranteed that the filtered information induces conscious will. Considering the possibility of unbiased sensory information, the internal influences still cannot be assessed, as cognitive processes will persist in biased ways.

Emotion, a strong and often imprecise factor that ignites positive or negative perceptions, obstructs the mind's ability to reflect critically. Emotions are involuntary and do not involve the act of the will to affirm or deny (Schmitter, 2021). Emotion serves as an essential motivating factor in shaping interpretations and perceptions, directly and indirectly affecting the process of belief formation. Beliefs are formed to align with the subject's current emotion or mood (Connors & Halligan, 2017). Without any deliberate or critical thought, explanations of sensory inputs that offer emotional benefits like comfort or certainty are more likely to be accepted as true and formed into a belief than equally plausible explanations that do not offer these benefits (Connors & Halligan, 2017).

Furthermore, individuals' identity and sense of self is a driving internal involuntary force. When confronted with contradictory information, individuals experience cognitive dissonance. Festinger (1962) describes cognitive dissonance as things that are not psychologically consistent with each other, like simultaneously holding conflicting beliefs. Dissonance reduction is then employed to reduce this uncomfortable mental state, involving rejecting or rationalizing information that challenges previous beliefs (Festinger, 1962). This impedes the genuine consideration and assessment of alternative viewpoints. However open and receptive anyone can be, the foremost concern of the mind is to avoid cognitive dissonance and maintain internal consistency.

While the prospect of gaining control over belief formation is appealing, thoroughly examining all sensory information entering the brain during belief formation is simply not feasible. Sensory inputs are filtered to reduce cognitive efforts- the mind can only consciously reflect on so much information (Schwitzgebel, 2021). With constrained attention and processing capacity, human cognition faces various limitations (Marois & Ivanoff, 2005). The mind is bombarded with an overwhelming amount of information daily, making it impractical to evaluate every piece of encountered information comprehensively. Consequently, even with the desire to change beliefs, the sheer volume and the flowing pace of information makes it challenging to uncover and assimilate all the relevant filtered information that could potentially alter beliefs.

Though the relationship between consciousness and will is not linear, the idea of changing mindsets can be drawn from this argument. Internal and external influences will invariably initiate and interfere with the formation of beliefs, but by changing perceptions of these influences, the maintenance and execution of beliefs can be controlled according to will. As the state of the world changes, individual realities transform with evolving thoughts. By acknowledging the hand-in-hand relationship between change and the involuntary, individuals can adopt an accepting mindset and choose how they perceive it. This prompts the development of a management system that can establish a standard for optimal and desired response to beliefs.

Conclusion

Beliefs play a fundamental role in shaping individuals' personal identity and influencing how they perceive and interact with the world around them. I have presented evidence supporting the involuntary nature of belief formation, stemming from internal



influences of cognitive biases and heuristics, and external influences of social and cultural conditioning. The impact of emotions and cognitive limitations further hinders the ability to consciously evaluate all incoming sensory inputs. Though the absence of complete control in forming beliefs is evident, I advocate for the development of an evolving mindset. As control is desirable and the removal of control is aversive for human beings, I emphasize that the will has the power to manage and execute beliefs. Just as it is adaptive in forming beliefs to automatically respond to the environment, it is equally crucial to appropriately modulate those responses within the given context. By acknowledging the involuntary aspects of belief formation and embracing the capacity to exert influence over beliefs, individuals can cultivate a mindset that fosters critical thinking, self-reflection, and the ability to adapt and evolve their beliefs. Ultimately, it is through this conscious effort of managing and executing beliefs that they can navigate the complexities of life and make informed decisions that align with their values and aspirations.

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Using a Systems Biology Approach To Reveal a Common Molecular Signature Across Neurodegenerative Diseases

By Kareem Fareed

Author Bio

Kareem Fareed is a senior at University School in Hunting Valley Ohio. He is passionate about neuroscience, as well as the application of technology and artificial intelligence in different areas of medicine. He plans to continue his work in these fields and utilize them in a future career as a neurosurgeon.

Abstract

Becoming increasingly prevalent in recent years, the three major neurodegenerative diseases - Alzheimer's (AD) Parkinson's (PD), and Huntington's (HD) - continue to avoid most attempts at treatment and early diagnosis. Operating under the same pathogenic umbrella of neuronal death, it stands to reason that these, and all other neurodegenerative diseases would share risk factors by virtue of their similar pathologies. The aim of this study is to analyze and compare the molecular signatures of the three neurodegenerative diseases, using a holistic approach, in order to uncover a common signature among them. To achieve this, three gene expression datasets are used, one for each disease. A molecular signature of each of the three neurodegenerative diseases at different genomic levels. The results of the overlap analysis point to common malfunctions in various autophagic, apoptotic, and mitophagic pathways. Locating a shared signature of the three diseases opens new avenues for drug repositioning across neurodegenerative diseases, offering novel ways of prevention and treatment and supporting future research toward precision medicine.

Keywords: Neurodegenerative, Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Bioinformatics, Systems Biology, Genetics, Convolutional Neural Network, AI, Neuroscience, Precision Medicine, Autophagic pathways, Apoptotic pathways, Mitophagic pathways, Overlap analysis, Genomic levels.



Introduction

Neurodegenerative diseases are a class of diseases marked by the progressive degeneration of neurons, the building blocks of the nervous system. These diseases often manifest as a decline in cognitive and motor function, severely impacting the quality of life for affected individuals. Parkinson's Disease, Alzheimer's Disease, and Huntington's Disease are prominent examples, each with unique pathophysiological features. The irreversible and progressive nature of these diseases makes early diagnosis and intervention crucial, hence requiring advanced informatics like deep learning and systems biology. Despite presenting varying symptoms, these three diseases share a very similar pathogenesis. It stands to reason that these, and all other diseases falling under the umbrella of neurodegeneration would share risk factors by virtue of their similar pathologies.

Parkinson's Disease (PD) is a neurodegenerative disease belonging to a group of diseases called Parkinson's Syndrome. There are two types of PD, hereditary etiology and sporadic etiology. Hereditary etiology is a result of a mutation in a specific gene, whereas sporadic etiology can affect anyone and occurs due to risk factors acquired during a patient's lifetime. PD appears with depigmentation and cell loss in the substantia nigra pars compacta (Figure 1) and the presence of Lewy bodies in the remaining nigral neurons (Bateman 2003). The loss of these dopaminergic neurons in the afflicted brain leads to many of the common symptoms of PD such as akinesia (the absence of voluntary or involuntary movements), rigidity (increased resistance to passive flexion or extension of a joint), and rest tremors (irregular movements in muscles when they are relaxed). With subtly progressing yet dangerous diseases such as PD, early diagnosis is of the utmost importance.

Alzheimer's Disease (AD) is the sixth leading cause of death in the United States and the only one among the top ten that cannot be cured, prevented, or treated. The number of people affected by AD is projected to reach 8.4 million by 2030 and the projected cost associated with dementia is estimated to be \$1.1 trillion by 2050 (AA, 2023). Similar to other neurodegenerative diseases, AD progresses silently for many years before the onset of symptoms. The silent preclinical stage of the disease is characterized by the accumulation of amyloid beta $(\alpha\beta)$ plaques outside the cell and intracellular neurofibrillary tau tangles in the brain.

Huntington's Disease (HD) is an autosomal dominant neurological condition caused by a single defective gene on chromosome 4 (NCBI). The degeneration of neurons in HD primarily causes motor issues, cognitive decline, and psychiatric problems. Motor symptoms often include jerky and uncontrollable movements known as chorea (Roos 2010). Cognitive decline manifests as difficulty in organizing tasks or coping with new situations, and over time it progresses to severe dementia. Psychiatric problems vary from depression and mood swings to more severe disorders such as obsessive-compulsive disorder and bipolar disorder. Like those mentioned above, HD has no cure. The disease progresses over 10-25 years and ultimately has life-threatening complications.

Neurodegenerative diseases have a complex nature as multiple modifiable, non-modifiable genetic, and non-genetic factors contribute to the diseases. This calls for the use of multiple modalities for neurodegenerative disease detection and prognosis, which are superior to single-modality methods. Autophagy has been shown to be a common factor in the progression of Alzheimer's, Parkinson's, and Huntington's (Guo et al. 2017). Autophagy is the cellular process of degrading or 'recycling' cellular components, and in failing, can lead to one of the above diseases. Such macroscopic-level commonalities tend to make biological sense. However, these biologically-implied similarities aren't easily visible on a more microscopic level.

Many statistical and computational methods have been developed for predicting the development and speed of progression of neurodegenerative diseases from the preclinical stage. Deep learning methods have been at the forefront of such efforts. For example, many Neural Network-based models, like Conventional Neural Networks and generative adversarial networks, have been developed and tested on magnetic resonance images of subjects with early symptoms, like memory concerns or mild cognitive impairment, with varying prediction accuracies (Reas et al. 2023, Qu et al. 2023, Zadeh 2023).



Other methods based on calculating polygenic risk score (PRS) from the subject's genotype data have been used to analyze susceptibility to developing the disease (Wightman et al. 2021). PRS is the product of statistical methods that have proven useful for disease prediction and prognosis, especially when combined with other biomarkers; however, it has limitations. The score calculation is heavily dependent on significant single nucleotide polymorphisms that are defined in the study and do not incorporate rare variants, which limits its ability to capture the whole genomic picture of the disease, especially if the condition is polygenic. Like all complex diseases, synergistic and non-linear interactions must be captured while computing the genetic risk factor of neurodegenerative diseases, which cannot be accounted for using PRS since it assumes linear, additive relationships. Moreover, PRS is more sensitive to the lack of diversity in the data. For example, the majority of available AD data is for subjects of European ethnicity while the disease is more prevalent in Asian, Hispanic, and African ethnicities (Matthews et al. 2018).

Every level of genetic data, going from the finest granularity to the coarsest, gives a different perspective on the underpinnings of the disease. Integrating multi-level omics data (e.g., genomic, transcriptomic, proteomic, epi-genomic) is a promising way to shed light on biological pathways beyond the potential of a single layer of omics data. Thus, the integration of omics data and the use of a holistic systems biology approach is warranted to get a comprehensive view of the underlying mechanisms of neurodegenerative diseases.

Methods

ND Gene Expression Datasets	# Cases	# Controls	# Screened Genes	# DE Genes	Significance Threshold (P-value)
Alzheimer's Disease (ADNI)	270	259	4,952	251	< 10 ⁻⁶
Parkinson's Disease (PPMI)	260	256	188	21	< 10 ⁻⁶
Huntington Disease (GEO)	109	88	198	15	< 10 ⁻⁴

Table 1. Descriptive statistics of the Neurodegenerative Disease (ND) datasets used in this study

Differential expression analysis was performed on each of the three gene expression datasets (Table 1) representing the three diseases under study. Using DESeq2, differentially expressed genes for each disease were chosen for downstream analysis (Love 2014). Differentially expressed genes were filtered at a high statistical significance of false discovery rate (FDR) of 0.2 and minimum fold change (FC) of 2 (p-value $< 10^{-2}$). Then the genes of each disease were mapped to biological functions using WebGestalt for enrichment analysis of the disease-associated gene sets (Zhang 2005). Biological process terms were used and the FDR threshold was set to 0.2. The resulting gene set for each of the three neurodegenerative diseases was fed into NetworkAnalyst (Xia 2014) for disease-associated tissue-specific Protein-Protein Interaction network analysis and visualization and for pathway analysis using the Kyoto Encyclopedia of Genes and Genomes (Kanehisa 2000). Significant protein interactions (PPI) and functional pathways were filtered at a p-value < 10⁻² and the FDR threshold was set to 0.2.

NetworkAnalyst is a web-based tool for statistical and network-based meta-analysis of gene expression data that outputs statistically significant PPI networks that harbor the differentially expressed genes from each gene expression dataset. For example, from the AD gene expression dataset, functional enrichment analysis was performed on the differentially expressed genes, and then the resulting gene set was fed into NetworkAnalyst for AD-associated hippocampusspecific PPI network analysis (The brain hippocampus was chosen in this case since it is known to be the first tissue significantly affected by AD). The intersection of the three disease-associated PPI networks, the output of the three neurodegenerative disease datasets, was computed using NetworkAnalyst. The resulting PPI network, at the intersection of the three disease networks, thus represented the common signature across the three neurodegenerative diseases.

Overlap Analysis

To characterize the functional overlap between the biological functions that are identified to be significantly associated with the three neurodegenerative diseases, based on the subjects of the three disease datasets, the pairwise overlap ratio is computed as the fraction of common significant biological function (genes, protein interaction networks, pathways) in every two diseases among the number of significant biological function in the two diseases (i.e., Jaccard coefficient).



Validation

Permutation tests were used to test the statistical significance of the results of the overlap analysis. First, a gene pool was created. For each study, the genotyping array model was identified. All RefSeq transcripts for hg38 assembly were downloaded from the UCSC Table browser and extended 100kb upstream and 10kb downstream and Refseq IDs were translated to HGNC symbols. All HGNC symbols matching Refseq IDs were combined and duplicates were removed. The final HGNC list served as the gene pool for random gene sampling. Gene sets are then randomly sampled such that the size of each set matches that of the observed gene set for each disease. The point of this was to generate a nonsensical dataset that shouldn't have any significant relationships.

A thousand permutated data sets were created with a permuted set size for each population matching the original data set. In each permutation, permuted overlap ratios were calculated as described in the overlap analysis. This resulted in 1000 matrices of pairwise overlap ratios between the three cohorts corresponding to each permuted data set. The mean values of the overlap ratio across all permutations were calculated. These calculations were then used to visualize the overlap in permuted datasets and assess the significance of the observed overlap (p-value < 10-2). The analysis of the permuted datasets should show less overlap as compared to the overlap analysis performed on the original dataset.

Results

The overlap analysis across the three neurodegenerative diseases revealed commonalities at the network level. Figure 1 illustrates the calculated commonalities between the three diseases at two different granularities. The overlap between the three diseases noticeably increased from gene (Figure 1.a) to network analysis (Figure 1.b). For example, there was minimal (1% between AD & HD and 2% between AD & PD) pairwise overlap at the gene level, but the overlap increased at the network level (Figure 1). The network-level analysis captured 23% overlap between AD and PD, 16% overlap between AD and HD, 11% overlap between PD and HD, and 2% overlap between the three, originally disjoint, disease datasets.

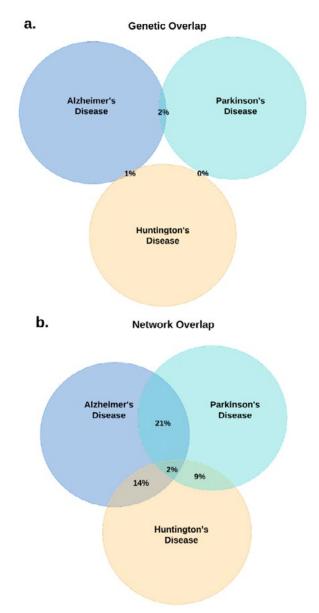


Figure 1. a. represents the Gene-level genetic overlap between the three diseases. b. displays the network-level analysis overlap between the three diseases. This figure highlights that despite displaying very little overlap at the Gene level, network analysis revealed a significant overlap between the three diseases providing a clearer picture of the commonalities between the diseases.

The significance of the overlap was visualized in heatmaps in comparison to their permutated counterparts in Figure 2 (p-value $<10^{-2}$). The permuted dataset (bottom row) showed no significant overlap



among the diseases indicating that the overlap found on the original dataset (top row) was significant. Permutation tests were done on both levels of overlap, genetic (left column) and network (right column).

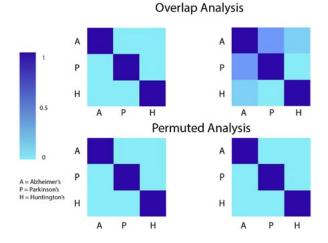


Figure 2. Pairwise overlap between the three neurodegenerative diseases with the gene-level overlap (left) and the network-level overlap (right). The computed pairwise overlaps between the neurodegenerative diseases (n=3). The correlation matrices were n x n matrices of pairwise overlaps between cohorts computed as the Jaccard Coefficient of similarity. The bottom row shows the corresponding results from the permuted data sets, the mean overlaps of a thousand overlaps computed on a thousand permuted datasets. $p<10^{-2}$. The analysis of the permuted datasets shows less overlap as compared to the overlap analysis performed on the original dataset which indicates that the results were significant.

The common neurodegenerative disease PPI is enriched in neurodegenerative disease-associated pathways (Figure 3, Table 2). For example, the MAP3K7 gene (3.a) is enriched in the Autophagy– animal pathway which plays a major role in housekeeping wherein it helps cells remove damaged components and maintain homeostasis. The UBA52 gene (3.b) is enriched in the Mitophagy- animal pathway which eliminates damaged mitochondria. The NFKB1 gene (3.c) is enriched in the Apoptosis pathway which is used to get rid of cells that are either harmful or useless and is crucial to maintaining a functional organism. Finally, the MAPK8 gene (3.d) is enriched in all three pathways.

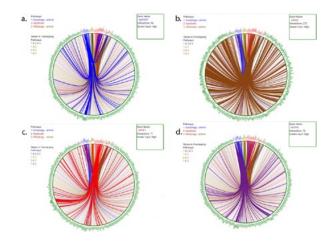


Figure 3. A Circos-visualized example of three significant Neurodegenerative disease pathways: 1. autophagy – animal 2. apoptosis and 3. mitophagy - animal, that were found significant in the datasets of the three diseases (Alzheimer's, Huntington's, Parkinson's) (Krzywinski 2009). The diagram shows interactions between genes enriched in the pathway mitophagy – animal in brown, interactions between genes enriched in the pathway apoptosis in red, and interactions between genes enriched in the autophagy - animal pathway in blue and interacting genes enriched in all selected three pathways in purple. All example genes were significantly enriched in their corresponding pathways and were found significantly expressed in the datasets of the three neurodegenerative diseases.

Pathway	p-value	FDR
Pathways in cancer	5.43×10^{-57}	1.73×10^{-54}
MAPK signaling pathway	9.00×10^{-48}	1.43×10^{-45}
PI3K-Akt signaling pathway	7.85×10^{-43}	8.32×10^{-41}
Focal adhesion	9.92×10^{-41}	7.89×10^{-39}
Ras signaling pathway	3.32×10^{-34}	2.11×10^{-32}
Hippo signaling pathway	1.77×10^{-28}	5.12×10^{-27}
Autophagy - animal	2.45×10^{-19}	3.00×10^{-18}
Apoptosis	5.06×10^{-16}	3.50×10^{-15}
Mitophagy - animal	3.57×10^{-9}	1.06×10^{-8}

Table 2. Pathway Enrichment Analysis on the overlap between the three neurodegenerative diseases (Alzheimer's, Parkinson's, and Huntington's). The table presents a sample of the common pathways that were relevant to the three.



Discussion

This study presents a comprehensive approach to understanding the molecular underpinnings of Alzheimer's, Parkinson's, and Huntington's diseases, using a robust differential expression analysis followed by network-based approaches. The significant findings from our analysis emphasize the complex yet potentially interconnected nature of these neurodegenerative diseases.

A key finding from the study is the minimal overlap at the gene level but a more substantial intersection at the network level between the diseases. This suggests that while the genetic underpinnings might be distinct, these diseases may converge at the network and pathway levels. The permutation tests further validated the significance of these overlaps, suggesting that the observed intersection is not a product of random chance.

Another significant aspect of our findings is the common malfunctions in autophagy, mitophagy, and apoptosis pathways among the three diseases. The central role of the MAP3K7, UBA52, MAPK8, and NFKB1 genes across these pathways suggests its potential as a universal component in the pathogenesis of these conditions. This discovery opens new therapeutic avenues, particularly in the realm of precision medicine.

Conclusion

This study highlights the shared and distinct molecular mechanisms underlying Alzheimer's, Parkinson's, and Huntington's diseases. The results of the overlap analysis revealed the genes MAP3K7, UBA52, MAPK8, and NFKB1 as common markers between the three diseases. They are implicated in autophagy, mitophagy, and apoptosis. Although this paper developed a molecular signature across three neurodegenerative diseases, the analysis could be made more robust through replication analysis using different datasets of the same diseases. The next steps would also be to test this signature against other neurodegenerative diseases like amyotrophic lateral sclerosis (ALS), Lewy-body dementia, and multiple sclerosis (MS) to see if they share the same signature. Then, the molecular signature of the diseases should be used as the target for a drug that can be used against all three diseases. In conclusion, this research opens up possibilities for the development of treatments that could be effective across different neurodegenerative conditions, marking a significant advancement toward more effective and personalized treatment approaches in the future.

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The Effectiveness of Loss Framing and Fear Appeal in Motivating Climate Action

By Minna Xu

Author Bio

Minna Xu is a junior at The Madeira School in Virginia. She is passionate about the environment and advocating for more formal climate change education.

Abstract

Current climate change communication involves various forms of framing: outcome framing, attribute framing, and point-of-reference framing. The focus of this paper will be on loss framing, a type of outcome framing. Past research on loss framing, including fear appeals, generally agrees that loss framing leads to suppression and denial of climate change information. This study aimed to determine whether fear appeal, a type of loss framing, effectively motivates people indirectly affected by climate change to take action. This review paper analyzed the results of 11 papers found on August 26, 2023, on ScienceDirect, with the keywords "climate change," "fear appeal," and "media" filtered for research articles. The results indicated that the papers reviewed generally found that either loss framing is effective on its own, loss framing is effective with specific solutions, that the effectiveness of loss framing may vary, or that motivational framing is more effective. This paper concluded that, generally, loss frames are more effective than motivational frames, but the effectiveness depends on the specific situation and group. There is a gap in the research concerning the effectiveness of loss framing climate change media, specifically on people indirectly experiencing climate change.

Keywords: Fear appeal, climate change, message framing, loss framing, pro-environmental behavior, outcome framing, climate action, media



Introduction

Since the 1800s, climate change, referring to "long-term shifts in temperature and weather patterns" (United Nations, 2023), has become increasingly anthropogenic, fundamentally due to the burning of fossil fuels. When burned, fossil fuels release greenhouse gases covering the Earth, trapping inside heat and raising temperatures (United Nations, 2023). Rising temperatures intensify extreme weather events such as droughts, heat waves, and large storms (Environmental Protection Agency, 2023). There is also severe biodiversity loss as climate change has become the greatest threat to coral reef systems (Suess et al., 2024), leading to warming waters that cause coral bleaching and microorganism growth. Furthermore, hurricanes and storm surges can lead to widespread damage to the already weak reef systems - damages well beyond the level that coral reefs can recover from (Gouezo et al., 2019).

To mitigate the effects of climate change, 175 countries signed the Paris Agreement of the United Nations Framework Convention on Climate Change, which proposed to hold global temperatures 2°C above pre-industrial levels, with 1.5°C being optimal. However, even if every country that signed the Paris Agreement met its national goals, there would still be a much greater warming of 3.2°C above pre-industrial levels. The Intergovernmental Panel on Climate Change (IPCC) - the part of the United Nations dedicated to studying the science behind climate change - published in its Sixth Assessment Report in 2021 that global surface temperature had reached 1.1°C above 1850-1900 temperatures in 2011-2020 (Calvin et al., 2023). The problem is that climate change is a global, collective problem requiring everyone to take action (Kundzewicz et al., 2020). The uncertainty of it also requires effective communication to motivate people to cut down on emissions (Kundzewicz et al., 2018).

What has become increasingly important to cutting down emissions is the communication of climate action to the general public. The environment is advertised to the public through various forms of media: films, news articles, social media, and the internet. Such advertisements can potentially motivate climate and sustainable actions (VanDyke & Tedesco, 2016). Environmental media is particularly useful

in convincing the public to recognize and engage in environmental protection (Ketelsen et al., 2020). However, it is impossible to present information about climate change neutrally without any context, so the way information is framed is crucial; it can place greater emphasis on an issue so that the audience can easily identify why the issue matters to them (Spence & Pidgeon, 2010). The most cited definition of message framing is "selecting some aspects of a perceived reality and mak[ing] them more salient in a communicating text, in such a way as to promote a particular problem definition, causal interpretation, moral evaluation, and/or treatment recommendation" (Entman, 1993). Combined with specific characteristics of the target audience, message framing can "substantially enhance adoption intentions for the advocated behavior" (Nab et al., 2020). This research was primarily concerned with investigating outcome framing, a type of message framing.

Outcome Framing

In outcome framing, the goal of the message is framed in terms of gains or losses. However, there are two different proposed explanations and effects of outcome framing. In the context of Amos Tversky and Daniel Kahneman's prospect theory, the effectiveness of either gain or loss framing depends on how risky it is to behave that way (Levin et al., 1998). When a behavior is risky, using a loss frame is more effective, whereas if the behavior is seen as safe or less risky, using a gain frame is more effective (Levin et al., 1998). Segev et al. found that under the assumption that pro-environmental behavior (PEB) is a preventive behavior, using a gain frame is more effective, which is in congruence with prospect theory. The other explanation is based on negativity bias, which asserts that negative messages are more impactful than equally positive messages (Spence & Pidgeon, 2010). Based on negativity bias, loss frames would be more effective. Fear appeals are a type of loss framing because they emphasize negative consequences (Tannenbaum et al., 2015). These appeals emphasize a threat to produce an "extreme emotional response" (Wilson et al., 1988). In the context of climate change media, fear appeals are warning-based, environmentally shocking, and pastoriented, depicting disastrous outcomes due to past unsustainable actions (Shen et al., 2020). Experimental evidence from psychology suggests that fear framing



is effective in causing many different behavioral changes. The greater the level of fear, the greater the behavioral change (Spence & Pidgeon, 2010). Another study (Groenendyk & Banks, 2014) argues that fear increases cognitive vigilance, which helps individuals adapt to threats. However, this behavior is dropped if the threat cannot be resolved. Even though fear fuels individuals to think about a problem, this does not lead to enough collective action to tackle climate change. Some have even argued that fear-inducing messaging does not lead to any action but the suppression and denial of climate change information (Janković & Schultz, 2017). When the stressor is portraved as uncontrollable, as in the case of fear appeals, it can lead to maladaptive coping, such as denial and giving up (Folkman et al., 1986), and it can harm the credibility of the message (Bults et al., 2011). The view that fear appeal leads to suppression of climate change information aligns with findings from evolutionary and psychological research, which state that suppression is a way to cope with uncertainty, a fear that would otherwise obstruct daily activities (Schaller & Crandall, 2004). Stennet (Stennett, 1957) suggests that there might be an optimal level of fear to motivate climate action.

The current research tried to investigate primarily 1) the effectiveness of loss framing, especially fear appeal, in eliciting pro-environmental behaviors in people indirectly affected by climate change and 2) if there are other factors, in addition to outcome frames, that affect climate change messages.

Methodology

The papers reviewed in this study were collected on August 26th, 2023, through ScienceDirect, a peer-reviewed journal article database. They were filtered to include only research articles with the keywords "climate change," "fear appeal," and "media." The search yielded 51 research articles, 40 of which were discarded because of irrelevancy to this study: their research primarily focused on investigating the impact of message framing on people directly affected by climate change, renewable or sustainable energy, risk communication about COVID-19, or had no mentions of the media's role in motivating climate action. All the papers were summarized. The main results on fear appeal were analyzed and grouped into four categories based on their position on the effectiveness of fear appeal.

Results

This review found that out of the 11 papers analyzed, the most common findings were that 1) loss frames, including fear appeals, are effective in motivating climate action (27.27%) 2) loss frames paired with specific solutions to climate change are effective (27.27%) 3) there are situations when loss frames are more effective than gain frames and vice versa (18.18%) 4) motivational messaging is more successful than fear appeal framing (18.18%).

Loss frames are effective on their own

A study conducted by Howell (2011) measured viewers' responses to the film The Age of Stupid, which presents a dystopian future devastated by climate change and highlights the problems with current fossil fuel dependency. The film uses a fear appeal narrative and does not explicitly give viewers answers on how to respond to issues raised in the film or how to lobby politicians. The study utilized a pre/post-test approach where a questionnaire was given to viewers to obtain their initial opinions before they watched the film. After, two post-test questionnaires were sent out: one immediately after the film and one 10-14 weeks after to test whether the film had lasting effects and inspired viewers to take action. In the second questionnaire, the study asked participants whether their concern had increased: 17.4% replied "No", 30.3% ticked "Yes, a bit" and 52.3% stated "Yes, a lot' (Howell, 2011). On the last questionnaire, participants demonstrated more action: 4.4% more people had donated money to a climate change organization in the past year. However, these actions required less effort, money, or time. Despite popular views that fear appeal media leaves people overwhelmed, this study found that respondents left the film with increased motivation to take action and felt more empowered to do so. The results could be argued to show the considerable success of fear appeal films, as 11.7% of respondents reported cutting down on driving and 8.6% on reducing their meat consumption (Howell, 2011). However, this could just reflect changes in social norms. The findings also cannot be generalized to the public as the participants represent a group highly concerned with climate change who took action even before the study.



Another study by Booysen et al. (2019) investigated household behavioral responses to droughts communicated through official announcements on water restrictions and public mentions of the topic on social media. In 2017, Cape Cod became notorious for the prospect, "Day Zero," that it would run out of municipal water. In response, from November 2016 to February 2018, the City of Cape Cod Town implemented six water restrictions from Level 3 to Level 6B (Booysen et al., 2019). After the city publicly announced the disaster plan, there was a stream of alarmist articles in the media, voicing their distrust in the policy. Water usage fell for three weeks following the media surge. The usage then decreased during the second week of December, consistent with the slight increase in media coverage. Social media and search term analysis found that the three-phased disaster plan that warned of dire outcomes elicited the biggest response from users, not restrictions or tariffs. Although inciting fear was risky, the study argued it may have been "the single most successful intervention in effecting profound behavioral change amongst citizens" (Booysen et al., 2019).

The final study by Shen et al. (2020) that found results in favor of fear appeals had the goal of researching how to make green advertising campaigns more effective. The study found that advertising appeal has a significant effect on attention. More attentional resources were used in processing warning-based appeals than vision-based ones, implying an advantage for warning-based appeals. They increase people's environmental concerns and pro-environmental value orientation, potentially leading to pro-environmental behaviors (Shen et al., 2020).

Loss frames are effective when the audience is given specific solutions

The main objective of a study conducted by Suess et al. (2024) was to find the effect of fearappeal media on participants' emotions and following intention for pro-environmental behaviors. Three 2-4 minute fear-appeal video message treatments were used to measure participants' intention to donate to coral reef restoration efforts. There were three conditions: Condition 1 included a high level of threat messaging and reassurance messaging, Condition 2 included a higher level of threat messaging with a lower level of reassurance messaging, and Condition 3 included a lower level of threat messaging and a high level of reassurance messaging.

Emotional responses were self-reported immediately after watching and measured using 11 items on 5-point bi-polar scales. The data was collected from the U.S. public from a panel on Qualtrics, which stores a database of over 30 million panelists who self-select to participate in different studies. Self-selection bias was minimized by sending out screening questions that randomly assigned participants to a survey without telling them the topic. The study found that the highest donations observed were in Condition 1 and 2, where higher proportions of threat messaging were included (Suess et al., 2024). Arousal, a salient driving force of donation intentions, also increased in Condition 1 and 2, but threat appraisal was only significantly associated with arousal in Condition 2 (Suess et al., 2024). Negativeaffectivity (negative emotions) emotional responses were related to increased donation intentions among videos where the ratio of threat-messaging was higher. However, this relation was not found in fear-appeal videos with higher ratios of reassurance messaging. In contrast, copping appraisal was associated with arousal in all conditions: arousal was significantly higher in conditions that included solution-oriented messaging. Another interesting link was that participants who had vacationed in a coral reef destination showed high levels of stated donations, \$2.62 more in Condition 1 and \$1.66 more in Condition 3, than those who had never vacationed in a coral reef destination. The study concluded that video messaging should introduce threats before presenting solutions.

In another study, 1182 Australian residents sourced by Qualtrics responded to a survey that assessed a broad range of participants' values, beliefs, and affective responses in the context of climate change. Participants were first presented with messages categorized based on the absence of six qualities, including direct reference to climate change, specific advice on taking action, and strong negative emotive content promoting adaptive responses to climate change in Australia. After viewing, participants were assessed on whether the messages led to perceptions of threat, efficacy, rejection, or intentions to adapt. The results indicated that there were three audience segments: alarmed (34.4%), which were people engaged in more adaptive behaviors and expressed the most support for climate change funding; uncommitted (45.2%), which were people engaged in more adaptive behaviors and were



more supportive for climate change funding than the dismissive group; and dismissive (20.3%) about climate change (Hine et al., 2016). The effect of the messages varied depending on whether the audience was alarmed, uncommitted, or dismissive about climate change; even subtle variations in messages lead to drastic differences in responses. However, consistent across all three audience segments was that providing specific adaptation advice and negative emotive content were "significantly associated" with more adaptation (Hine et al., 2016).

Effectiveness of Frames Vary

In a study focusing on attribute and outcome framing in the context of climate change, 161 psychology students completed a series of questions about climate change where they were presented information from IPCC's (2007) fourth assessment report in terms of losses or gains and local or distant impacts. The results indicated that, directly, gain frames produced higher perceived severity of the impacts of climate change and more positive attitudes toward mitigation than loss frames (Spence & Pidgeon, 2010). Indirectly, loss frames produced more fear responses, increasing perceived severity and higher recall of information. This, in turn, led to a positive association with attitudes toward climate mitigation. Nonetheless, gain frames are more effective when fear responses and information recalled are controlled. There is a systematic advantage in presenting information in a gaim frame, with results consistent with prospect theory (prevention behaviors are construed as low risk, so gain frames better prompt them).

(Nab et al., 2020) conducted a study that used outcome framing (emphasizing gain versus losses) and point-of-reference framing (emphasizing benefit for self versus. for the environment) to see whether they can positively influence, in both the short-term and the long-term, homeowners to use more sustainable energy solutions. In this study, environmentally significant behaviours were considered to be investing in insulation and alternative heating systems. The study found that short-term intention to invest in alternate energy is higher in a self/loss condition than in self/gain and higher when the message is presented in a gain frame to someone with a promotion focus. However, when the message is presented to someone with a preventative focus, loss frames yield higher short-term intentions to invest (Nab et al., 2020). Neither the outcome frame nor the point of reference affected message effectiveness directly. This finding was consistent with the results found on long-term intention.

One article on adaptive coping, which are ways people can manage stress whilst still having good well-being (Mah et al., 2020), suggested that there is no right way to communicate climate change. Still, there are general rules that can be followed to have more effective communication. If messages want to incorporate fear appeals, they should also state the severity of the threat, the individual's likelihood of being affected, and what they should do to mitigate it. Messages should embrace uncertainty; instead of focusing only on the worst-case scenario, messages should present multiple scenarios and their possible solutions. Interventions designed to increase people's capacity to cope should be customized for a target audience because people have constant ways to cope that will impact how they deal with climate change stressors. There is no single way to effectively communicate adaptive coping, as no single climate change stressor impacts everyone to the same extent. Not only are there variable stressors, but also variable individual responses and coping. There must also be adaptive coping mechanisms designed for individuals and a collective group because individual, community, and ecosystem resilience are essential to the collective resilience to climate change. So, messages should not burden the individual but instead find ways that the community can adaptively cope.

Loss frames are less effective than motivational frames

The last predominant result was that motivational or gain framing is more effective than loss framing in promoting climate action. In a study measuring the influence of motivational or sacrifice framing on perceived "competence, engagement, and behavioral intentions" (Gifford & Comeau, 2011) for home and transportation-based mitigation behaviors, 1038 residents of Ontario, Canada, were recruited through a random sample purchased from a commercial polling organization. The results showed stronger perceived competence, climate change engagement, and intentions to change behavior over the next year with motivational framing (Gifford & Comeau, 2011). If messages cannot target a specific



population, there is more value in using motivational messages.

Another study specifically focused on atmosfear, which is the use of discursive practices to scare people into taking climate action that can influence decision-makers to be more likely to act in favor of mitigating climate change. The study concluded that the negative framing of atmosfear can be counterproductive in many ways (Kundzewicz et al., 2020). Negative framing overemphasizes extremes and does not inform people of the risks.

This research paper has presented the existing literature on the effect of fear appeal media about climate change on people indirectly affected by climate change. Fear appeal is effective to a certain extent in motivating pro-environmental behaviors indirectly. However, the extent to which they are effective needs to be studied more as they appear to vary depending on the targeted group, the form of media, with what variable they are studied in relation to (such as point-of-reference framing), and the type of climate action measured. There is more research done on the effect of message framing on people directly affected by climate change (flood risk communication, earthquake mitigation, et cetera) than on people indirectly affected. There is insufficient research on people indirectly affected by climate change (those who hear about it on the news or see campaigns about it) or specifically fear appeals. Our research has generally reached the same conclusion as existing wider literature on the effects of fear appeals in the media on motivating climate action.

Discussion

The literature reviewed reveals that, in general, loss frames, including fear appeals, are effective in motivating climate action. However, the extent to which they are effective depends on the target audience. If fear appeals were to be used more, they should focus on targeting people with preventative focuses and highlight the individual benefits of engaging in climate action. Importantly, there should be specific solutions presented alongside fear appeals. Nonetheless, there is insufficient research to reach a consensus on the effectiveness of fear appeals in the context of climate action. There is a significant gap in the research on climate messaging, and each review paper seemed to focus on a different aspect of loss framing. It is important that more research is conducted on what messages are effective in motivating pro-environmental behavior because climate change will only affect the world more in the future. There should be a curriculum implemented to teach the population the definition of anthropogenic climate change and the knowledge they need to adapt and mitigate its effects.

Conclusion

This literary review paper explored whether loss framing media is effective in motivating people not directly affected by climate change to take action and whether there are other factors that contribute to the effectiveness of climate media. One main finding was that loss framing is effective in motivating proenvironmental behavior on its own. Another major finding was that loss framings are effective when paired with specific solutions to take climate action. Other findings include the following: the effectiveness of loss framing varies with individual variables, and the focus of the media and motivational framing is more effective than loss framing. Overall, there is insufficient research to reach a consensus on the effectiveness of loss framing, specifically fear appeal, in promoting climate action.

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Changes in the Brain During Menopause: A Comprehensive Review

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Abstract

Menopause is a natural physiological transition marked by fluctuations in hormone levels in the body, resulting from a decline in ovarian function and eventual ovulation cessation, not a complete halt in ovarian production, which is closely tied to menstruation (World Health Organization, 2022). Not only is it a physiological change, but it's also considered a neurological change, as indicated by key symptoms that appear, such as cognitive decline, sleep disturbances, and altered mood (Thomas, 2021). These symptoms are all related to lobes and regions in the brain. In previous years, there has been various in-depth scientific research into menopause and changes in the brain, which has provided valuable insights for this review article. The objective of this paper is to explore the relationship between menopause and neurological changes, emphasizing the impact of hormonal fluctuations on cognitive decline, sleep disturbances, and mood alterations, and providing a foundation for holistic interventions that prioritize women's well-being during this natural life transition.

Keywords: Neuroscience, menopause, brain, hormones, ovaries, cognitive behavioral therapy, cognitive impairment, vasomotor symptoms, mood swings, estrogen



Introduction

Menopause is the phase in women's life when they experience the permanent cessation of menstrual periods, which is also commonly known as "the change of life" (Johns Hopkins Medicine). The decline in ovarian production marks the end of a woman's reproductive ability, which usually is when a woman hasn't had any menstruation for a consecutive year. In the United States, around 1.3 million women undergo menopause annually, with the typical onset between the ages of 51 and 52. Even though some women start to experience early menopause between the ages of 40 and 45. The ages of onset may differ among different races and ethnicities as previous research suggested. For example, Black women usually experience menopause 8.5 months earlier than White women (Meissner, 2022).

Menopause is often accompanied by vasomotor symptoms (VMS), such as hot flashes, night sweats, heart palpitations, and fluctuations in blood pressure. The primary explanation for the emergence of these symptoms during menopause is the impact of hormonal fluctuations on the mechanisms governing blood pressure and temperature regulation. Interestingly, the causes of hot flashes are probably neurovascular, meaning they occur when alterations happen in the segment of the nervous system responsible for circulation. Experts theorize that hot flashes emerge from modifications in the brain region responsible for regulating body temperature (Nall, 2023). These episodes may be triggered by a sudden decrease in estrogen, which is a key hormone that plays a role in maintaining cognitive well-being, bone health, cardiovascular system function, and various vital physiological processes (Nichols, 2023). However, the majority of people know estrogen for its role in female reproductivity (Nall, 2023).

The fluctuations in estrogen levels have a significant impact on various brain regions that could be the leading cause of vasomotor symptoms. If estrogen levels rise or decline abnormally, the hypothalamus cannot regulate body temperature correctly, which directly results in the occurrence of hot flashes. Inactivation of the brainstem, which is the connection point of the brain and spinal cord, could be the reason for sleep disturbances during menopause for women. In addition, the amygdala is part of the limbic system that acts as the emotional center and controls explicitly fear and anxiety. The inefficiency of estrogen may increase neuronal excitability, thus there will be several mood swings (Thomas, 2021). As estrogen level falls, women are likely to experience a growing sense of forgetfulness, also known as mental "fogginess". Interestingly, low estrogen levels are also associated with the decline in gray matter volume, which is found to have an impact on Alzheimer's Disease and other forms of dementia such as vascular dementia (LCMC Health, 2023). This topic is significant because menopause is one point along the continuum of women's life stages, marking the conclusion of their reproductive years (World Health Organization, 2022).

Discussion

Hormonal Influence on Brain Changes

The menopausal transition is closely linked to subtle cognitive decline. The impacts vary from classical nuclear actions to nonclassical membranemediated effects, estrogen traditionally regulates gene transcription through its interaction with nuclear receptors. The brain is closely connected to the reproductive system and women's ovaries via the HPG axis (hypothalamus pituitary-gonadal), which is responsible for releasing ovarian hormones and regulating reproductive activity (Nielsen and Herrera, 2017).

According to a multi-modality neuroimaging study of women at different menopause transition stages (pre-, peri-, post-), menopause transition demonstrates a significant impact on the structure, connectivity, and metabolic characteristics of the female brain during the hormonal and neurological changes of the midlife. By scanning and using neuroimaging techniques in the brains of more than 160 women between 40 and 65 who were in different stages of the menopause transition (MT), the researchers examined the blood flow, structure, metabolism, and function. The brain regions responsible for cognitive functions are the most affected at all ages. However, it's crucial to note that it's hard to draw the boundary between changes from aging or menopause, which could be a focus for future menopause research (Mosconi et al., 2021).



The rapid alteration of neuronal and pituitary cell excitability triggers pathways like cyclic adenosine monophosphate and mitogen-activated protein kinase. This influences the function of receptors such as kainate, G-protein coupling, calcium channels, and calcium ion entry, offering neuroprotection against damage caused by excitotoxins and free radicals (Conde et al., 2021). In the realm of estrogen, there are 3 common types: Estrone (E1), Estradiol (E2), and Estriol (E3). Estradiol (E2), crucial during the menopausal transition, exhibits the highest affinity for intracellular estrogen receptors and binds strongly to the membrane-associated G protein-coupled receptor known as GPR30/GPER1. This hormonal shift during menopause, however, shows limited evidence of varying the risk of developing Parkinson's disease. Estradiol's impact extends to cognitive aging, quality of sleep, and mood stability, with associations found in multiple neuropsychiatric disorders, such as Alzheimer's Disease, schizophrenia, and depression. Evidence suggests that E2 plays a significant role in protecting dopaminergic neurons, with potential implications for Parkinson's disease. Furthermore, research links estrogens to cognitive aging through three factors: the cholinergic system, the dopaminergic system, and mitochondrial dysfunction. The cholinergic system's correlation with cognitive aging is supported by reduced cholinergic acetyltransferase activity. This hypothesis of the cholinergic system's correlation with cognitive aging also arises from Alzheimer Disease's treatment, particularly the FDA-approved acetylcholinesterase inhibitors. These drugs function to elevate synaptic acetylcholine levels and promote cholinergic signaling overall. Multiple literature studies have pointed out the significance of the dopaminergic system for cognitive aging (Russel et al., 2019). Its significance is evident in diseases like Huntington's disease and Parkinson's disease, where imbalances correlate with cognitive abnormalities (Brown and Marsden, 1988). Poor cognitive performance has been suggested by brain imaging scans such as Positron Emission Tomography (PET) that in individuals carrying the Huntington's disease mutation, there is a correlation between the level of striatal dopamine receptor binding and cognitive performance, where reduced binding is associated with poorer performance (Lawrence et al., 1988). Unlike the cholinergic and dopaminergic hypothesis, the mitochondrial aging hypothesis proposes that as mitochondria age, increased mitochondrial DNA Damage results in elevated reactive oxygen species,

leading to decreased mitochondrial activity and signs of aging. Applied to cognitive aging and Alzheimer's disease, it links elevated reactive oxygen species for neurofibrillary tangles and Alzheimer's hallmarks. Alzheimer's progression involves reduced brain glucose uptake, which shifts from aerobic to anaerobic metabolism, together with changes in glucose utilization preceding clinical symptoms. Mitochondrial dysfunction precedes age-related cognitive deficits. Studies on estrogen's effects reveal decreased glycolytic gene expression in irregularly cycling animals, resulting in a shift toward mitochondrial function, fatty acid uptake, and ketone metabolism (Russell et al., 2019).

Psychological and Cognitive Effects

Individuals with objective cognitive impairments on neuropsychological assessments while maintaining their ability to perform daily life activities independently, are known to live with Mild Cognitive Impairment (MCI). Common symptoms are having difficulty memorizing, learning, concentrating, and making decisions. The incidence of Mild Cognitive Impairment (MCI) was 4.5% among 6.376 postmenopausal women observed over 5.4 years in the Women's Health Initiative Memory Study (WHIMS). However, there has been limited research on the connection between MCI and menopausal factors. Cognitive functioning in postmenopausal stages exhibited a trend toward decreased performance when compared to pre- and perimenopausal phases, especially in domains such as verbal delayed memory and executive functions (cognitive control and supervisory attentional system). These cognitive domains are believed to be more responsive to fluctuations in estrogen levels. The Study of Women's Health Across the Nation (SWAN) assessed a group of 2,362 American women for four years through the repeated administration of neuropsychological tests, which is significant due to its great contribution to the understanding of women's health in areas such as menopausal transition, hormonal changes, cardiovascular health, psychological well-being. Women's performance on both immediate and delayed memory assessments during both early and late perimenopausal phases didn't exhibit any improvement with repeated testing. Likewise, Kilpi et al. conducted research involving 2,411 middle-aged women in the United Kingdom, confirming a decline in processing speed and immediate and delayed verbal



episodic memory during the perimenopausal phase. Furthermore, alterations in verbal episodic memory performance exhibited correlations with folliclestimulating hormone and luteinizing hormone levels. Follicle-stimulating hormone (FSH) is produced by the pituitary gland at the base of the brain, and is released mainly for sexual development and reproduction. As a result, it impacts the functioning of both ovaries and testes (Cleveland Clinic, 2023). Overall, the menopausal transition has a profound impact on the female brain, impacting brain structure and function from hormonal fluctuations to cognitive decline.

Interventions and Therapies

Currently, many methods of interventions could be used to reduce menopause-related symptoms. Among them, are hormone replacement therapy (HRT), cognitive behavior therapy (CBT), and antidepressants which will be discussed in this review paper (Mayo Clinic, 2023).

Hormone Replacement Therapy (HRT), also known as postmenopausal hormone therapy or menopausal hormone therapy (MHT), is a broad term used to describe unopposed estrogen in women who have had a hysterectomy and the combined estrogen-progestin in women with an intact uterus, necessitating progestin to prevent estrogen-related endometrial hyperplasia. This medical approach is utilized to supplement a woman's diminished natural estrogen and progesterone hormones during and after menopause. This treatment is often suggested by healthcare professionals to relieve common symptoms that occur during this transition such as hot flashes and vaginal dryness. Additionally, it's employed to address long-term physiological changes, such as osteoporosis (bone loss), associated with the decline in estrogen and progesterone levels (National Cancer Institute, 2023). To alleviate menopause-related symptoms, conventional hormone replacement therapy (HRT) involves using both estrogen and progesterone components to mimic the natural hormones produced by the ovary. There are various types of estrogen therapies available, including those that are naturally occurring in the human ovary such as estradiol and estriol (Harrison and Shanahan, 2023). Still, HRT has its downsides and limitations for certain populations. If patients encounter blood clots, cancer (e.g., breast, uterine, or ovarian), heart, liver, gallbladder disease, heart attack, known or suspected pregnancy, stroke,

or unexplained vaginal bleeding, a professional may recommend avoiding HRT (WebMD Editorial Contributors, 2023). Some of the common downsides are hot flashes, night sweats, weight changes, osteoporosis, mood changes, gastrointestinal (GI) symptoms, vaginal and menstruation change, and more. Discussing with the healthcare professionals regarding the patient's prescription before using HRT is vital. This conversation should address anticipated side effects, strategies for mitigation, and procedures to follow if the patient encounters unforeseen side effects (Cancer Net, 2023).

Other non-hormone therapies aim to address the emotional challenges experienced during menopause and related issues, such as Cognitive behavioral therapy (CBT). It is a common form of psychotherapy where the patient collaborates with a mental health counselor in a structured manner. CBT's objective is to enhance patients' awareness of pessimistic thought patterns, enabling them to gain a clearer perspective on challenging situations and develop more efficient responses (Mayo Clinic, 2019). To help people cope with stressors from menopause, CBT manages problematic hot flashes and night sweats. According to a study in 2018 by Hardy et al., 124 women aged 45 to 60 who were experiencing a minimum of 10 episodes of hot flashes and night sweats were randomly divided into two groups. One group was asked to use a booklet of CBT self-guided techniques to cope with their symptoms, while the other group of participants had no treatment waitlist control. The group that used the booklet showed an improved sense of well-being compared to the other group. By breaking negative thought patterns, people who incorporate CBT into their approach may find relief from symptoms of depression and anxiety. Incidentally, CBT could help people who suffer from sleep disruptions sleep better during perimenopause and menopause. Despite the advantages of CBT, there are some disadvantages as well. For example, attending CBT sessions consistently takes up a lot of time. Because of CBT's organized format, it might be a good choice for individuals with more sophisticated mental health requirements or learning challenges. Other critics contend that as CBT primarily deals with present concerns and concentrates on particular issues, it may not explore potential root causes of mental health conditions, such as a distressing childhood (The CBT Clinic).



The final intervention that will be introduced in this review article is antidepressant medications, which is highly recommended for people with hot flashes who cannot take estrogen. There are different types of antidepressants, including selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and monoamine oxidase inhibitors (MAOIs). SSRIs and SNRIs are the class of medications prescribed most often for treating depression and hot flashes that are common for menopause. As the first-line treatment for depression, they provide comparable benefits to other medications while minimizing safety concerns and side effects (Rush, 2022). A comprehensive review reveals that these medications (SNRIs and SSRIs) lead to a substantial decrease in both the frequency and intensity of hot flashes. For instance, desvenlafaxine (a type of SNRI) demonstrated a remarkable 62% reduction in hot flash occurrences, equivalent to seven fewer incidents daily, and an overall 25% decrease in their severity (Stubbs et al., 2017). SSRIs function by inhibiting the reabsorption of serotonin by the bloodstream, resulting in elevated serotonin levels in the brain, which can enhance depression. It's important to note that SSRIs enhance the brain's existing serotonin supply rather than stimulating increased production, so they cannot boost the low levels of serotonin in the body (DiGiacinto and Fink, 2023). Nonetheless, the side effects of SSRIs and SNRIs should be taken into consideration when prescribing them. SNRIs have the potential to increase blood pressure, requiring regular blood pressure monitoring (Weer et al., 2013). Due to the varying side effects and effectiveness of SSRIs and SNRIs, if one of these medications proves ineffective or poorly tolerated, an alternative drug can be prescribed (Ferguson, 2001). Notably, patients should avoid combining MAOIs with other antidepressants such as SSRIs, as this combination can lead to serotonin syndrome, a condition that can be life-threatening (Laban and Saadabadi, 2023).

Conclusion

Based on various research conducted or studied about menopause and the brain, menopause, marking the permanent cessation of menstrual periods, occurs around ages 51-52 in the U.S., with an annual occurrence of 1.3 million women undergoing this significant transition. Vasomotor symptoms (VMS) like hot flashes, night sweats, and blood pressure fluctuations arise from hormonal shifts impacting temperature and blood pressure regulation together with menopause. Research indicates a correlation between estrogen decline (hormonal fluctuations) and alterations in gray matter volume, potentially linking menopause to cognitive disorders such as dementia. Furthermore, the menopausal transition is connected to cognitive decline, and neuroimaging studies reveal its impact on the brain structure, connectivity, and metabolic characteristics of the female brain. Interventions for menopause-related symptoms involve Hormone Replacement Therapy (HRT), Cognitive Behavioral Therapy (CBT), and antidepressant medications like SSRIs and SNRIs, each offering advantages but implications at the same time to symptom management. Understanding the interconnection between hormonal changes, cognitive decline, and effective interventions is crucial for supporting women's overall well-being. Despite the effectiveness of current treatments/interventions for treating menopause-related symptoms, these methods entail risks for occurrence or complications after the surgery. As a result, future research may concentrate on reducing the effects of menopause and minimizing associated complications for intervention options. Ongoing research in the field of menopause aims to deliver enhanced therapies for health across communities and healthcare settings.

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Kavain Hydroxylation in Kava Metabolism: Computational Analysis

By Youlin Feng

Author Bio

Youlin recently graduated from high school and has a strong passion for chemistry. When his friend at school introduced him to the drink, kava, he became fascinated by its properties and decided to carry out research using computational chemistry methods. He hopes to study chemistry and conduct more projects in this field in the future.

Abstract

Kava, a non-alcoholic beverage derived from the Piper methysticum plant, commonly also known as kava, has a prominent role in the cultures of Oceania due to its calming and soothing effects. These psychoactive properties have sparked interest beyond Oceania and in the scientific community, who see potential for medicinal applications. However, alongside these beneficial effects, consumption of kava has been linked to potential hepatotoxicity, raising safety concerns. Understanding the cause of this hepatotoxicity requires a detailed exploration of kava's metabolic processes, specifically those involving kavain, its primary constituent. Recent studies have found the hydroxylation of kavain to 12-hydroxykavain as a key step in kava's metabolic pathway. Yet, the precise mechanism of this conversion and the hydroxylation intermediates involved remain poorly understood. To address this knowledge gap, our study employed Spartan, a computational chemistry software, to model the hydroxylation process. We analyzed the stability and chemical properties of the proposed reaction intermediates, providing a detailed view of this critical phase of metabolism. Our analysis reveals that three of the five proposed intermediates appear stable, suggesting they may play significant roles in the hydroxylation process. This finding also enabled us to narrow down the possible reaction pathways of hydroxylation. Having a better understanding of the key step of kava metabolism could guide the development of safer, more effective kava-based products, balancing the therapeutic potential of kava with a reduced risk profile.

Keywords: kava, kavain, hydroxylation, iron porphyrin, metabolism, hepatotoxicity, reaction intermediates



Introduction

Oceania is a term used to describe the island communities of the Pacific Ocean: Polynesia, Micronesia, and Melanesia. Oceania was one of the few communities without alcoholic beverages by the time of first contact with Europeans in the 18th century (Singh, 1992). Instead, these Pacific Islanders consume their own staple beverage kava, which is prepared by grinding the roots and stalks of the kava plant Piper methysticum (Chua et al., 2016). Piper methysticum grows abundantly in the islands of Polynesia and are believed to originate from Melanesia (Tarbah, 2004). Kava drinking is an integral part of Pacific Islander culture, often being the centerpiece for religious rituals, acting as a lubricant for solemn gatherings, serving as a daily social drink, or for medicinal purposes (Lebot & Lèvesque, 1989).

The preeminent role of kava in Oceania is largely attributed to its outstanding pharmacological properties, and also the belief that drinking kava restores strength, soothes stomach pains, and cures ailments (Builders, 2019). Kava displays psychoactive properties, particularly soothing and calming effects (Soares et al., 2022), but it is not classified as a drug since its consumption leads to neither addiction nor dependency (Lebot & Lèvesque, 1989). Due to these properties, kava was used in Germany before World War I to manufacture various medicines, and Europe also used kava as a treatment for cystitis, gonorrhea, and gout around the same period (Singh, 1992). In recent decades, the scientific community and Western countries have also shown interest in kava due to its potential to treat cancers (Freeman et al., 2023) and symptoms associated with anxiety (Geier & Konstantinowicz, 2004) and stress-induced insomnia (Wheatley, 2001).

However, recent research has linked heavy consumption of kava with hepatotoxicity (Fu et al., 2008) and unexplained liver injury (Humberston et al., 2003). The mechanisms leading to hepatotoxicity are still unclear but are known to be related to the metabolic processes of kava in the human body (Soares et al., 2022). One possible suggested mechanism is related to the formation of activated metabolites that induce hepatotoxicity (Fu et al., 2008). However, before this mechanism related to hepatotoxicity can be identified, it's important to first understand how kava is metabolized in the human body. Kava undergoes several metabolic steps within the human body, the major one being the hydroxylation of kavain, the kavalactone found in the highest concentration in kava (Tarbah et al., 2003). This research paper aims to investigate this hydroxylation step in the metabolic pathway of kava, specifically aiming to understand how kavain is converted to 12-hydroxykavain, which is the main kavain metabolite found in both blood and urine (Tarbah et al., 2003). Through studying this hydroxylation step, it is hoped that there will be a greater understanding of kava metabolism in a human body which may aid in finding the mechanism leading to hepatotoxicity for future research.

Composition of kava

The pharmacological properties of kava are thought to be primarily due to a group of compounds named kavalactones (Cairney et al., 2002). The six most abundant kavalactones are kavain, dihydrokavain, methysticin, dihydromethystin, desmethoxyyangonin and yangonin (Figure 1), with kavain being the main kavalactone in kava (Chua et al., 2016). In the following sections, all carbon numbering related to kavain will follow the scheme presented in Figure 1.

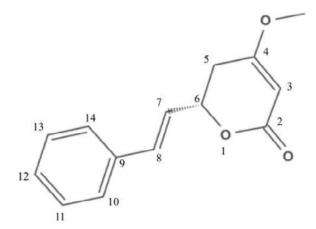


Figure 1. Skeletal representation of kavain molecule



Metabolism of kava

Köppel & Tenczer (1991) identified the following metabolites related to urinary excreted kavain in rats following oral administration: hippuric acid, p-hydroxybenzoic acid, 4-hydroxy-6hydroxyphenyl- 5-hexen-2-one, 4-hydroxy-6- phenyl-5-hexen-2-one, dihydrokavain, and 12-Hydroxykavain (Duffield et al., 1989), which also supported the findings by Rasmussen et al. (1979) who conducted a similar study. To see if there was any correlation between kava metabolism in rats and humans, Tarbah et al. (2003) performed a study on kavain metabolites in human urine after oral administration. Upon analysis, a different set of metabolites was identified in human urine compared to rat urine, but 12-hydroxykavain was a metabolite that was prevalent in human urine as well as rat urine. 12-hydroxykavain and its glucuronide and sulfate derivatives were also found in the highest concentrations in the urine samples. These findings suggested that hydroxylation at the C-12 position of the phenyl ring in kavain to form 12-hydroxykavain was a major step in metabolism of kavain (Figure 2). Wang et al. (2019) found that CYP2C19, a liver enzyme protein, was the primary enzyme responsible for kavain bioactivation and hydroxylation.



Figure 2. Hydroxylation of kavain to form 12-hydroxykavain

Aromatic Hydroxylation:

The possible mechanism pathways (Figure 3) for hydroxylation were found by Trager et al. (2007). The oxygen atom of the iron porphyrin attaches to the para position due to better resonance stabilization and less steric hindrance compared to the ortho position (Bathelt et al., 2004). The basis of this study will center around exploring the chemical properties of the five kavain hydroxylation intermediates depicted below (Figure 3).

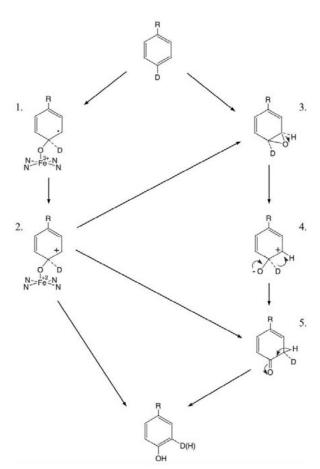
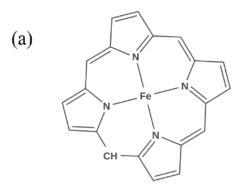


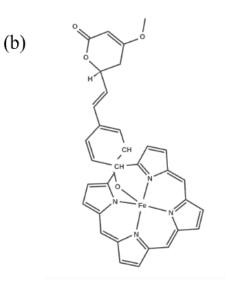
Figure 3. Possible mechanism pathways of aromatic hydroxylation of kavain adapted from Trager et al. (2007)

Trager et al. (2007) suggest that intermediates 1 and 2 are bonded to an iron porphyrin each. For this study, we used an iron porphyrin model derived from the National Center for Biotechnology Information (2023) (Figure 4a).

Figure 3 illustrates atom D as a hydrogen atom and R as the remaining components of the kavain molecule. Based on the same figure (Figure 3), we also inferred the hydroxylation kavain intermediates as follows:







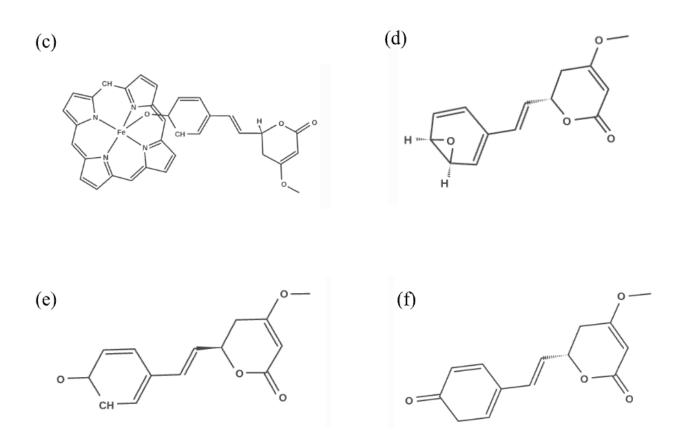


Figure 4. (a) Skeletal representation of iron porphyrin adapted from National Center for Biotechnology Information (2023). (b) Skeletal representation of Intermediate 1. (c) Skeletal representation of Intermediate 2. (d) Skeletal representation of Intermediate 3. (e) Skeletal representation of Intermediate 4. (f) Skeletal representation of Intermediate 5.



Methods

We used the Spartan program, a molecular modeling software developed by Wavefunction Inc., to model the hydroxylation intermediates in this study. The software offers various setups including Energy, Equilibrium State Geometry, Transition State Geometry, Equilibrium Conformer, Conformer Distribution, and Energy Profile. Each of these setups serves a different function and we used them in conjunction with semi-empirical quantum chemical models such as PM3, Hartree-Fock, density functional, and MP2 to calculate the lowest energy arrangement for a kavain-related molecule.

In this study, we chose the Equilibrium Geometry setup along with a PM3 calculation. We used the Equilibrium Geometry setup to calculate the lowest potential energy state in all dimensions of a specific hydroxylation intermediate. Equilibrium Geometry calculates the forces acting on each atom based on their potential energy surface and determines how to adjust the positions of those atoms to minimize the total potential energy. It then repeatedly adjusts the positions of the atoms until a local minimum on the potential energy surface is found, where the forces on all atoms reach approximately zero.

We chose PM3 because it was the most accurate calculation method applicable to systems with transition metals like the iron in the iron porphyrin used in this study. PM3 finds the most stable set of molecular orbital coefficients and then adjusts atom positions until it finds the lowest possible energy configuration. PM3 also involves approximations to the time independent Schrödinger equation H Ψ = E Ψ , which is the fundamental wave equation in quantum mechanics that calculates and provides an understanding of the energy levels and wavefunctions of a quantum system.

To create a hydroxylation intermediate, we either combined a pre-existing kavain molecule with an iron porphyrin or formed new bonds with oxygen/ oxide atoms and broke existing double bonds using the various bond manipulation functions within the program. We drafted the intermediate and then minimized its energy using the "E minimize" function before running it through the Equilibrium Geometry and PM3 calculation to ensure accuracy of the result. After completing the calculations, we analyzed the hydroxylation intermediates for any outstanding chemical traits. We used the "measure distance" and "measure angle" functions to analyze the geometry of the intermediates, and the Higher Occupied Molecular Orbitals (HOMOs) function and electrostatic potential map to assess any signs of atomic orbital overlap and electron density (Wavefunction Inc., 2011).

Results

Analysis of the reactant kavain and the product 12-hydroxykavain:

Kavain:

Kavain contains cyclic ester, ether, and phenyl functional groups. Although analysis of its electrostatic potential map showed that the highest electron density was found at the cyclic ester group (Figure 5a), the reactivity of kavain was found to mainly occur at the phenyl ring (Wang et al., 2019). This could have potentially been explained by analysis of HOMOs, which showed that there was strong atomic orbital overlapping and hence high electron density around the phenyl ring particularly at the para position (Figure 5b).

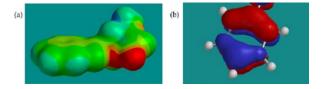


Figure 5. (a) Electrostatic potential map showing high electron density at cyclic ester group. (b) HOMOs showing overlapping atomic orbitals at phenyl ring

12-hydroxykavain:

Addition of a hydroxy group O-H at C-12 position added to the presence of orbitals around the ring (Figure 6a). Analysis of HOMOs also showed that there was strong electron density on one side of the oxygen atom despite significantly less density on the other side due to bonding with a hydrogen atom (Figure 6b). This illustrated that the oxygen atom in O-H was still prone to attack by electrophiles and



reinforced the finding by Tarbah et al. (2003) that described 12-hydroxykavain existing in its glucuronide and sulfate forms.

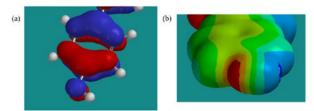


Figure 6. (a) HOMOs showing atomic orbitals at oxygen of O-H group. (b) Electrostatic potential map showing strong electron density at the oxygen atom from the O-H group.

Chemical Analysis of the Five Hydroxylation Intermediates:

Intermediate 1:

A strong feature of Intermediate 1 was the relatively close proximity between the iron atom of the iron porphyrin and C-11 of the phenyl ring, with a distance of 2.113Å. This short distance suggested that there was potentially some form of bonding between the two atoms. This hypothesis was further reinforced upon analysis of the interactions between the HOMOs of atoms where there was an evidently large atomic orbital overlap (Figure 7a). This bonding was significant in that it also dictated the orientation of the kavain molecule as it bonded with the iron porphyrin molecule. It also seemed to affect the way in which the oxygen atom of the iron porphyrin attached to the kavain molecule, which can be seen through the bond angle of 97.47° around the oxygen atom of the iron porphyrin (Figure 7b).

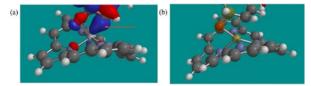


Figure 7. (a) HOMOs showing atomic orbital overlap between C-11 and iron atom. (b) Bond angle around oxygen.

Intermediate 2:

Intermediate 2 also shared similar features to Intermediate 1. The distance between the C-11 atom of the phenyl ring and the iron atom was 2.029Å, which was a shorter distance than that found in Intermediate 1. This suggested an even stronger form of bonding between the two atoms. However, the bond angle around the oxygen atom measured at a larger angle of 99.08° than Intermediate 1. These two findings were slightly contradictory in that it was hypothesized that a shorter distance and thus stronger bonding would also lead to a smaller angle. The bond lengths measured around the oxygen atom of the iron porphyrin were almost identical to those in Intermediate 1, so the nuance in bond angles must have been related to some other factor. Upon analysis of HOMOs, there was a significant atomic orbital overlap spanning across from C-11 atom of the phenyl ring to the iron and oxygen atom of the iron porphyrin that was not found in Intermediate 1 (Figure 8). This orbital overlap could be a possible explanation for the different bond angles; however, more future research into this area is still needed.

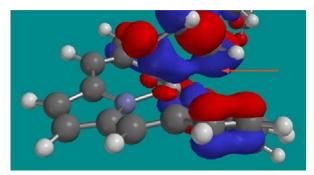


Figure 8. HOMOs showing significant atomic orbital overlap between C-11, iron and oxygen atoms

Intermediate 3:

The main feature of Intermediate 3 was the triangular arrangement of the oxygen atom and the two adjacent C-11 and C-12 atoms of the phenyl ring. There was a cis arrangement where both hydrogens on the C-11 and C-12 carbons were on the same side. The bond angles were all relatively close at 58.40, 58.46, and 63.14° while the distance of C-11 to oxygen and C-12 to oxygen were both approximately 1.440Å, showing that it could have almost been considered as an isosceles triangle (Figure 9). Considering how close the atoms were to each other and the isosceles



triangle formation the atoms were in, this arrangement seemed rather unstable and unlikely to exist in human conditions.

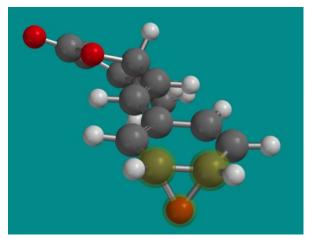


Figure 9. Isosceles triangular arrangement between C-11, C-12 and oxygen atoms

Intermediate 4:

The most prominent feature of Intermediate 4 was the negatively charged oxide bonded to the C-12 atom. The bond angle between oxide, C-12 and C-11 (Figure 10a) measured 58.45° which appeared rather irregular. A possible explanation for this arrangement was through analysis of HOMOs, where the electron repulsion created by the two electron dense pi bonds in the phenyl ring (Figure 10b) forced the oxide into an awkward position. Additionally, it was interesting to note that this bond angle of 58.45° around this C-12 position practically did not change from the corresponding angle of 58.46° in Intermediate 3. The position of this oxide also prevented both the hydrogen atoms on C-11 and C-12 from remaining in planar positions (Figure 10c). Such an arrangement would likely be too unstable to exist under human conditions.

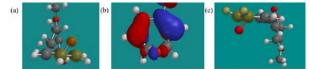


Figure 10. (a) Bond angle around C-12 atom. (b) HOMOs showing pi bond orbitals at phenyl ring. (c) C-11 and C-12 atoms with non-planar hydrogen atoms.

Intermediate 5:

Intermediate 5 contained a ketone group and appeared to be relatively stable.

Energy:

A comparison of the energy values (heats of formation) of the five intermediates was also recorded below (Table 1). Both Intermediates 1 and 2 had the most negative energy values while Intermediates 3 and 4 had the least negative. This further reinforced the instability of Intermediates 3 and 4.

Table 1. Energy Values of the five hydroxylation intermediates

Hydroxylation Intermediate:	Energy Values (kJ/mol):
Intermediate 1	-1023.42
Intermediate 2	-1013.04
Intermediate 3	-256.09
Intermediate 4	-254.15
Intermediate 5	-403.90

Discussion

After analyzing the Spartan calculations, Intermediates 1, 2 and 5 all seemed to be stable intermediates while Intermediates 3 and 4 were both unstable in their own ways and thus were unlikely to be viable intermediates that could exist in the hydroxylation mechanism. This was further reinforced by the fact Intermediates 3 and 4 had the highest set of energy values at -256.09 and -254.15 kJ/mol making them the most unstable (Table 1). Referring to Figure 3 with these findings in mind, the pathway involving Intermediates 3 and 4 can be ruled out, meaning that the remaining pathway of kavain to Intermediate 1 to Intermediate 2 to Intermediate 5 to 12-hydroxykavain would be more plausible (Figure 11a). Alternatively, another pathway would be kavain to Intermediate 1 to Intermediate 2 to 12-hydroxykavain which would not even require the ketone (Intermediate 5) to be formed (Figure 11b).



Having a stronger understanding of the metabolic pathway of kava and in particular its major hydroxylation step could provide hints to the cause of hepatotoxicity of kava ingestion. It is hoped that future studies on hepatotoxicity might use these findings on the suggested hydroxylation intermediates and mechanism pathway as a potential starting point for their research.

As for future research, experimental validation of these proposed hydroxylation pathways is needed. In vitro studies using human liver microsomes or in vivo studies using animal models could be performed to corroborate the findings from our computational analysis. Furthermore, the potential hepatotoxic effects of the metabolites produced during these hydroxylation processes should be investigated.

It would also be beneficial to investigate the specific role of the CYP2C19 enzyme in the hydroxylation process, as this could provide further insights into the metabolism of kava and possibly pave the way for the development of targeted interventions to modify this process.

Lastly, while this study focused on the hydroxylation of kavain, future research could also explore the metabolic pathways of the other kavalactones in kava to provide a more comprehensive understanding of its pharmacokinetics.

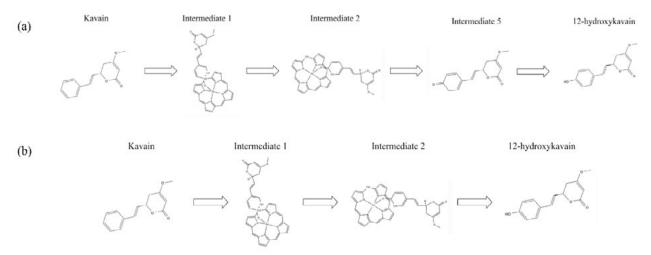


Figure 11. (a,b) Two proposed possible reaction pathways for the conversion of kavain into 12-hydroxykavain.

Conclusion

In this study, we utilized computational chemistry software, Spartan, to model the hydroxylation process of kavain, a key constituent of kava, a beverage integral to Pacific Island cultures. The aim was to gain insight into the potential hepatotoxicity linked with kava consumption, believed to be associated with its metabolic processes. Our investigation revealed that out of the five proposed intermediates involved in the hydroxylation process, three displayed stability, suggesting their significant roles in the process. This finding has allowed us to propose plausible reaction pathways for kavain hydroxylation.

While this study offers substantial insights into the metabolism of kava, it is important to note that the results are based on computational models which may not fully emulate the conditions in the human body. The intermediates modeled in our study might differ from those produced in laboratory synthesis, highlighting the need for further research involving both computational simulations and laboratory analyses. Despite these limitations, this research provides a more detailed understanding of the kavain hydroxylation step, a crucial phase in kava metabolism.



Although Tarbah et al. (2003) suggested a reaction pathway for the kavain intermediates found in the whole kava metabolism process, there is still yet to be any published studies related specifically to the hydroxylation mechanism and this paper is likely to be the first. We believe our findings will guide future studies aiming to identify the mechanism leading to hepatotoxicity, thereby contributing to the development of safer and more effective kava-based products. As research continues to unfold, it is crucial to bear in mind the cultural significance of kava in Oceania and the potential for its use in treating various health conditions. Therefore, a balanced approach is needed, one that respects cultural traditions while also considering potential health risks and benefits. This research signifies a step forward in our understanding of kava metabolism and provides a foundation for future studies in this important area.

Limitations

We used the Spartan program to simulate possible arrangements for the hydroxylation intermediates. However, these simulated arrangements may not match the intermediates produced by laboratory synthesis in future studies. Furthermore, the calculations we performed may not have fully replicated conditions in the human body. While we chose the Equilibrium Geometry setup as the most suitable for our study, the geometry optimization process might have constrained certain bond lengths and angles due to the theoretical assumptions inherent in the program.

The PM3 calculation was an approximation and might not have captured all aspects of the molecular behavior of the hydroxylation intermediates. More accurate representations of the intermediates might have been provided by Density Functional and Hartree-Fock calculations. However, due to the large size of the intermediates, the laptop we used could not process calculations more accurately than PM3. Future studies also using computational programs like Spartan should consider other forms of calculation as well and potentially compare the differences in the intermediates produced.

Wavefunction Inc. (2011) also did not provide any advice or suggestions for selection of different combinations of setups and calculations. Although we believe that Equilibrium Geometry and PM3 was the best combination for this study, we do not rule out the possibility that a different setup might have provided more accurate models of the hydroxylation intermediates.

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Conflict of Interest

The author of this paper states that there were no conflicts of interest <u>https://scholarlyreview.org/</u> <u>published-issues-1</u>

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