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Cover Photo: Cave salamanders (*Eurycea lucifuga*) are often found in the "twilight zone" area. This zone is near the entrance of the cave where a small amount of natural light still falls. *E. lucifuga* feed mainly on various insects and spiders. In the fall one might find their eggs in little crevices of rocks that have water/moisture in them or along rimstone pools. This particular specimen was found in Bluff River Cave scrambling around popcorn formations on the rocks.

About the Photographer: Amy Hinkle (Sunguramy Photography) holds a Master of Science and specializes in biochemistry and neuroscience research. She is also an avid caver and photographer and develops techniques to bring light to these pitch-black underground systems without the use of massive amounts of camera gear. Having always enjoyed the worlds of both art and science, she endeavors to join the two in both her photography and graphic design work. Both have appeared on covers of multiple scientific journals including *Neuroscience*, biotech company advertisements, and other publications.

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Research

Using Dissolved Organic Matter Fluorescence to Signal Changes in Carbon Cycling During a Cave Stream Experiment

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Cave ecosystems have detritus-driven food webs that obtain carbon and other nutrients from material that washes into caves. With no primary production and limited mechanisms for the entry of detritus and dissolved organic matter (DOM), caves are assumed to be energy and nutrient limited. To test the energy limitation hypothesis, a cave stream was amended with corn stover (leaves, stalks, and husks left over from corn harvest) for a year. Water samples were taken regularly and analyzed for nutrient chemistry and fluorescence of compounds in the DOM found in the water. Using PARAFAC, a statistical modeling analysis, we transformed fluorescence intensities of water samples to create a model with four components that characterized the composition of DOM in the stream. The fluorescent DOM components found during this experiment in the cave stream included humic-like material, organic compounds from microbial production, and amino acids. The addition of the corn stover ultimately led to a change in DOM composition, and an increase in microbial and invertebrate production was observed. In addition to DOM changes due to carbon additions, flooding in the cave ecosystem contributed to differences in fluorescence, and thus, water DOM composition. At times flooding masked the influence of the experimental carbon addition on DOM fluorescence, suggesting temporal variability associated with these events is an important regulator of carbon limitation.

Introduction

Some of the most biologically unique places on Earth are found in underground cave systems. Because caves do not receive any sunlight they do not harbor any photosynthetic primary producers and instead rely on secondary production by heterotrophic organisms. This heterotrophic production is performed by microbial communities in the stream and is passed up the food web to invertebrates (i.e. chironomids) and vertebrates (i.e. cave salamanders) when these animals eat the detritus (coarse dead organic matter and its associated microbes) with the bacteria and fungi (microbes) living on them. The cave food web is thus ultimately reliant upon detritus and dissolved organic matter (DOM) reaching the cave from the surface as a source of energy and carbon for growth [5]. One study found that dissolved organic matter (DOM) was the most important factor controlling the flux of energy in a cave system [3]. The lack of high quality sources of carbon has created a shortage of energy in cave systems, and this lack of energy may

control the trophic dynamics, the composition of communities, and even the evolution of native organisms [3].

DOM is a complex and heterogeneous mixture of small organic compounds derived from microbial, algal, and higher plant matter. It is produced during the breakdown of organic soil matter, the release of algal and zooplankton byproducts, the lysis of bacteria and algae, and the decomposition of macrophytes [6]. DOM plays a major role in aquatic ecosystems by regulating pH, attenuating light, and serving as a major nutrient and energy resource at the base of food webs [1]. Cave systems typically have limited DOM complexity considering that many of these carbon sources are not found naturally in cave systems. DOM composition in any ecosystem is influenced by watershed dynamics as well as local hydrological processes, but caves are the extreme case in this dependency [4]. Dissolved organic carbon (DOC) is ~50% of DOM, and serves as the basis for all organic life in the cave stream. It has been widely shown that there is a direct link between DOC and microbial biofilm activity.

With no primary production, stable temperature, and limited movement of organic matter, cave ecosystems and food webs are thought to be much more stable temporally than above ground systems. This hypothesis has been supported by studies that found microbial communities in karst environments (a geological distinction characterized by subterranean limestone caves that have been carved out by water) were temporally-consistent, regardless of the hydrological conditions [2].

The objective of this project was to assess the energy limitation hypothesis in cave ecosystems *in situ* by amending a single cave stream with additional carbon inputs. Corn stover, a mix of leaves, stalks, and husks from left-over corn harvest, was added to Bluff River Cave in northeastern Alabama for a period of one year. Corn stover is an ideal additive given its high carbon content. A control stream reach was established upstream of the corn addition, and corn stover was added downstream of the control reach. We focused specifically on the changes in organic matter chemical composition of stream DOM over the course of the experiment. The complexity of naturally-occurring DOM makes it difficult to characterize and study the constituent components using traditional chemical techniques [6].

Over the last two decades the use of fluorescence for characterizing DOM has been applied to terrestrial, marine, and anthropogenic-derived samples [6, 8, 1]. PARALLEL FACTOR ANALYSIS (PARAFAC) is a statistical analysis that was used to characterize the large data set of fluorescence intensities. PARAFAC is able to characterize DOM by separating out various unique fluorescing components found throughout the data set. PARAFAC analysis is now an important tool for characterizing DOM make-up, with various fluorophores and their relative concentration being tracked via changes in fluorescence intensity [6]. We predicted that the increased dissolved organic matter leaching from the corn stover would create observable differences in DOM fluorescence between the control and manipulation reach. The corn stover would supply the manipulation reach with a consistent and accessible source of carbon, and thus any natural variation (i.e. flooding) would be observed as changes in fluorescence in the control reach, but not in the manipulation reach. Changes in DOM composition were also predicted to result in altered water chemistry as well as increased production by the microbial community. This increased microbial activity was predicted to result in changes in food web dynamics due to the presence of more resources to be utilized by detritivores and predators.

Methods

Site Description

Bluff River Cave is a limestone karst cave located in Jackson County, Alabama. It features a 1000 meter(m) stream that runs through the cave, with its main source being an underground spring. The recharge area, or the area where rainwater percolating into the soil eventually reaches Bluff River, is mostly forested, minimizing the affects of urbanization. A 100m control reach was created 25m upstream of the 100m manipulation reach. Addition of the corn stover to the manipulation reach initially occurred on February 13, 2010, at a density of ~ 1000 g dry mass m^{-2} (Fig. 1).

Subsequent additions followed floods that washed out a significant portion of the corn stover. Natural coarse particulate matter was not expected to contribute to the carbon input of the stream as it is spring fed and there are no major cave openings except downstream of the experimental area. Bat guano was not expected to have a significant effect on the composition and concentration of DOC in the stream either, as there is a minimal population of bats in the cave system and most are found near the entrance away from the collection sites.

Sample Collection and Analysis

A total of 118 water samples (61 from the control reach, 57 from the manipulation reach) were collected between February 2010 and February 2011. Samples were taken at least monthly, and in the first four months samples were taken more frequently in order to capture short-term dynamics associated with the added stover. Samples were filtered in the field using combusted glass fiber filters (nominal poresize 0.7 μm). Three replicate samples from each reach were taken in the same spot. These filtered samples were kept on ice until in the lab, where they were used to measure DOC, NH_4 , NO_3 , total dissolved nitrogen (DON) and soluble reactive phosphorus on an ion chromatograph. Additional water samples were collected and filtered from both reaches and analyzed using fluorescence spectroscopy. These samples were stored @ 4°C to minimize microbial activity occurring in the lab that could alter the fluorescence of the sample. The samples were returned to room temperature before analysis on a Perkin Elmer LS 55 fluorometer and Shimadzu UV-1700 UV-Vis Spectrophotometer. Three-dimensional Excitation-Emission matrices (hereafter referred to as EEMs) were generated measuring fluorescence intensity of the liquid sample at different excitation wave-

lengths and emission wavelengths. Excitation wavelengths were from 240nm – 400nm in increments of 10nm, and emission wavelengths were from 350nm-525nm in increments of 2nm. The fluorescence spectra intensities were normalized to the area under the Raman peak at excitation wavelength 350nm of a water blank. To ensure that the only appreciable fluorescence found within a stream water sample was from the sample and not contamination associated with the cuvette, a “cuvette check” was performed before every sample run. A quartz-glass 1cm cuvette was thoroughly rinsed and filled with water and run on the LS 55 to determine overall cleanliness of the cuvette. If the fluorescence was below the pre-determined cut-off, then the cuvette was considered clean. Normalized water blank EEMs were then subtracted from each sample to remove Raman scattering due to the H-O bonds. To correct for instrument bias associated with the instrument’s specific optical components (inner filter effect), manufacturer-provided correction files for excitation and emission were applied to each sample [4]. Removal of both the inner filter effect and Raman scattering essentially removes instrument specific biases [7]. Sample absorbance was measured on the Shimadzu UV-spectrophotometer from 240nm-560nm in 1nm increments.



Figure 1: Bluff River Cave with the addition of corn stover

Data from the water sample EEMs were collected, compiled, and analyzed using PARAFAC analysis via MATLAB software. PARAFAC Analysis was performed with MATLAB Version 7.8. Code for MATLAB functions were provided by Dr. Rose Cory (University of North Carolina – Chapel Hill) and adjusted in-house as needed. Thirty samples (14 control reach, 16 manipulation reach) were removed from the data set as outliers, resulting in a final data set of 88 samples [7]. Validation of PARAFAC models was done via split-half analysis. The final set of data was divided into two random, equal sized groups, and then

each half was independently modeled. If the two halves had equal loadings, the model was assumed to be valid [7].

Results

Cave Hydrology and Chemistry

Over the course of this study there were 16 floods, with 11 occurring during the winter and spring months (December through May), and 5 occurring during the summer and fall months (June-November). Baseflow water depth averaged 0.6m, and water depth typically returned to baseflow levels 1-2 days after a flood event. The magnitudes of the floods were generally greater during the rainy winter and spring months, with the largest flood (January 2011) increasing water depth to 2.4m. After May of 2010, water level decreased during the summer and fall months to a low of 0.44m on November 6th (Fig. 2). Average water temperature for the winter and spring months was 12.9°C, and 13.8°C for the summer and fall months.

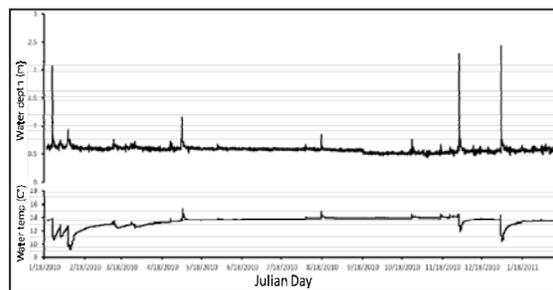


Figure 2: Water hydrology for Bluff River over the course of study

Differences in nutrient chemistry between the control reach and manipulation reach were not statistically significant for any measured compound when considering samples from the entire sampling period (Table 1).

However, the concentration of DOC was also compared between the two reaches for the drier months of June 2010-November 2010. If two DOC measurements from two dates were removed, the DOC in the manipulation reach was statistically greater than the DOC in the control reach. Data were also collected on the population of higher-trophic level invertebrates and vertebrates. There was an increase in the abundance of invertebrates throughout the course of the study in the manipulation reach, where the carbon addition from corn stover occurred, but there was no change in the control reach [Michael Venarsky, personal communication].

PARAFAC Model

Four fluorescence components were identified using our PARAFAC model and their relative abundances in each water sample were assigned. Contour plots for each component allow characterization of those fluorophores (Fig. 3).

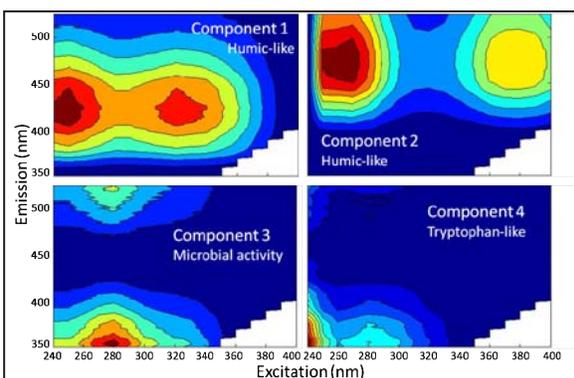


Figure 3: Contour plots for the four validated components by PARAFAC.

Component 1 contains two major peaks, both with highest emissions between 410-440nm, and one with an excitation maximum at 260nm and the other with an excitation maximum between 300-340nm. Based on similarities in our data and previously published work, the peak at excitation maximum 260nm represents UV humic-like fluorophores, and the peak between 300-340nm excitation represents visible humic-like fluorophores [7].

Component 2 contains two fluorescence peaks, both with emission between 450-500nm. One of the peaks is at excitation 240-280nm, and the other peak is 360-400nm. These values of fluorescence have not yet been identified in the literature as being associated with a specific fluorophore. Given the similarity in patterns found with Components 1 and 2, we concluded that the fluorescence of Component 2 may also be a humic-like material.

Component 3 showed an excitation maximum at 280nm, and an emission maximum at 360nm. This same component was identified in other studies and is thought to represent biological production within the water column [7].

Component 4 fluoresces at an excitation maximum of 250nm and emission maximum of 380nm. This has been characterized as the fluorescence of the indole ring structure in the amino acid tryptophan [7]. Tryptophan fluorescence intensities can be used to characterize the general concentration of proteins and other amino acids in the sample, as they have been found to be correlated [8]. For presen-

tations of results we show the relative contribution of each component (1-4) to the total fluorescence in the sample (Figure 4).

Correlations between the components allow trends to be observed between different fluorophores that suggest different sources for these components. Component 1 and Component 2 were positively correlated ($p=0.002$, $r^2=0.303$), while Component 1 and Component 3 were negatively correlated ($p<0.000$, $r^2=0.440$). Component 4 was negatively correlated with Component 3 ($p=0.026$, $r^2=0.171$). This suggests that Components 1 and 2 were derived from a similar DOC source, and that when this carbon source brought C1 and C2 into the cave stream, it did not bring C3, but rather diluted the concentration of C3. The negative relationship between Components 3 and 4 also suggests that they were derived from different sources.

To determine whether the addition of corn stover influenced chemical composition of DOM in the manipulation reach, we compared the component percentages between the two reaches. During the wet winter and spring months of 2010, the variability in DOM composition due to flooding (described below) masked differences between the two reaches. However, statistical differences between the control and manipulation reach were apparent during the drier months (June 2010-November 2010). The percentage of Component 3 in the samples was lower in the manipulation reach than in the control reach during these months, while the percentage of Component 1 was higher in the manipulation reach. Component 2 was equal between the two reaches. Between June 2010 and November 2010 Component 4 was positively correlated with DON ($p=0.070$, $r^2=0.446$).

Raw values of fluorescence for each EEMs component were also compared between the two reaches during these dry months, and it was found that the only component that showed differences in raw fluorescence between the control and manipulation reach was Component 3, but this was not statistically significant due to low statistical power. Raw fluorescence of Component 1 was almost identical between the reaches, but because total raw fluorescence remained the same with a decline of fluorescence in Component 3, the component percentage of Component 1 increased. Dissolved organic nitrogen (DON) in the manipulation reach was correlated with Component 4 during the dry months, and this relationship was not found in the control reach.

Flooding in the cave during the wetter months resulted in greater changes in DOM composi-

tion than were anticipated. We predicted that in the manipulation reach there would be less variation in response to floods because the corn stover would be a large source of carbon; however, this prediction was not supported by experimental results. There was variability in the component percentages associated with flooding events for both the control and manipulation reach. A decreasing exponential relationship was observed between DOC and the number of days since the last flood, and this relationship was significant for both the control ($p=0.031$, $r^2=0.386$) and manipulation reach ($p=0.032$, $r^2=0.455$). This suggests that flooding brought new DOC into the cave that was slowly “pushed out” as the flood water moved through the ecosystem. When EEMs data from both reaches were combined, Component 1 was negatively correlated with DOC.

Discussion and Conclusion

As the study progressed, the DOM composition as well as the food web dynamics in the manipulation reach proved to be influenced by the addition of the corn stover. Whether it was from a decrease in flooding or time needed to saturate the water with DOM, from June 2010 – February 2011 there were observable differences in DOM composition between the two reaches. As discussed above, the concentration of the Component 1 fluorophore, or humic-like material, remained largely stable between the two reaches throughout the dry period. There was a real decrease of Component 3 fluorophore, or microbial production byproducts, in the manipulation reach after June 2010. During the dry months, without floodwater DOC overshadowing DOC leaching from the corn stover, the heterotrophic organisms in the manipulation reach had more access to the DOC leaching from the corn stover, and greater secondary production ensued in the manipulation reach. This production travelled up the food web and led to an increase in the population of invertebrate consumers and vertebrate predators, who exerted top-down control on the microbial community. Due to consumption of microbes by predators, as well as higher microbial activity in the manipulation reach in response to the corn addition, the microbes living in the manipulation quickly took up the fluorophore of Component 3 in the manipulation reach and turned it into living biomass, which was then consumed by invertebrates. Essentially, the DOC from corn stover became trapped in the upper trophic levels of the food web as predicted. The positive correlation between Component 4 and DON in the manipulation reach during the dry months also suggests an increase in production. The minerali-

zation of the corn stover added more nutrients to the stream, which were again quickly taken up during microbial production. The nutrients were utilized in the formation of amino acids, which Component 4 can be used to estimate. As dissolved organic nitrogen increased, so did Component 4, or amino acids.

Samples taken at times of high flow exhibited fluorescence in both reaches that were overshadowed by flooding effects. This result is contrary to our prediction that natural variation such as flooding would not be observed in the manipulation reach due to the large, stable source of DOC from the corn stover. Instead, DOC concentration in both reaches was negatively correlated with flooding, suggesting that caves can indeed be susceptible to hydrological processes that bring in large amounts of DOM not seen during low flow periods.

Additional Figures:

	Phosphate (µg/L)	Ammonium (µg/L)	Nitrate (µg/L)	DON (mg/L)	DOC (mg/L)	C1 (R.U. & %)	C2 (R.U. & %)	C3 (R.U. & %)	C4 (R.U. & %)
Control Reach (High flow)	10±2	5±4	228±78.9	0.04±0.03	5.4±2.5	0.0833 ±0.04 593 7.3%	0.0618 ±0.00 873 33.3%	0.0479 ±0.00 850 25.1%	0.0123±0.014 4 4.3%
Manipulation Reach (High flow)	9±3	6±6	190±63.6	0.057 ±0.033	6.2±2.9	0.0728 ±0.01 45 36.7%	0.0653 ±0.01 24 33.0%	0.0470 ±0.00 754 24.3%	0.0120±0.008 9 5.8%
Control Reach (Low flow)	9	5±2	300	0.13	2.8±1.8	0.1306 ±0.07 72 38.7%	0.0984 ±0.04 03 34.4%	0.0616 ±0.02 27 21.8%	0.0233±0.020 15 4.9%
Manipulation Reach (Low flow)	8	5±2	253	0.062	4.0±2.1	0.1370 ±0.07 14 39.8%	0.1190 ±0.05 91 35.1%	0.0674 ±0.02 71 21.0%	0.0143±0.009 3 4.1%

Table 1: Concentrations of nutrients within each reach and between the rainy and low-flow seasons. In addition, averages for components in Raman Units (a measure of fluorescence intensity) and average component percentages.

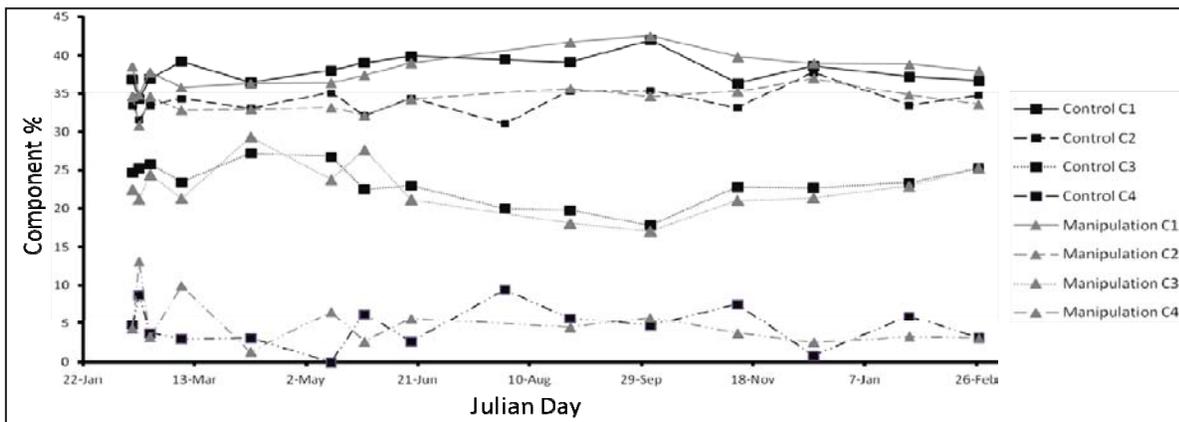


Figure 4: EEMs component percentages versus the calendar day. Component percentages are averages for each sample date.

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Dining Hall Diversity: Assessing Segregation in University of Alabama Dining Halls

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Each year the University of Alabama makes statements about diversity on campus, but in a city that is the home to former governor George Wallace's famous "Stand in the Schoolhouse Door", have students integrated? By observing who sits with whom among students on campus, this study examines the facts of segregation on the University of Alabama campus. Over the course of four months, 1132 students were observed dining in 487 groups in campus dining halls. These students were classified according to race and gender, and the demographic breakdown of their tables were recorded. These data were analyzed using SPSS statistical software to determine the overall levels of integration, as well as which demographic categories were most and least likely to sit at a table integrated by race or gender. Of the 1132 students sampled, we observed 571 males and 561 females, 281 African American Students and 851 Caucasian or other students. 11% of all the individuals were observed sitting in racially integrated groups. Specifically, we saw 8.9% of females sitting in integrated groups, 13% of males sitting in integrated groups, 9% of Caucasian or Other students sitting in integrated groups, and 16% of African American individuals sitting in integrated groups.

Introduction

It seems a bit odd that 58 years after *Plessy v. Ferguson* was overturned by *Brown v. The Board of Education of Topeka*, thus ruling "equal but separate" facilities for public education unconstitutional, that we would still be addressing issues of segregation on the campus of a public university. Certainly we have come a long way since Chief Justice Warren said:

"We conclude that, in the field of public education, the doctrine of "separate but equal" has no place. Separate educational facilities are inherently unequal. Therefore, we hold that the plaintiffs and others similarly situated for whom the actions have been brought are, by reason of the segregation complained of, deprived of the equal protection of the laws guaranteed by the Fourteenth Amendment."

Brown v. Board of Education, 347 U.S. 483 (1954) (USSC+)

347 U.S. 483

Argued December 9, 1952

Reargued December 8, 1953

Decided May 17, 1954

Nevertheless, segregation is still a part of daily life for many people, and its effects can be damaging, often leading to prejudice and stereotyping [1]. In their paper, *Recent Advances in Intergroup*

Contact Theory, Pettigrew and Tropp conducted a meta-analysis of 515 studies and over 250,000 subjects in which they demonstrate that intergroup contact typically leads to a decrease in prejudice [4]. Their analysis indicated that intergroup contact is effective at reducing prejudice not just among racial groups, but also among other groups, specifically mentioning homosexuals, the disabled, and the mentally ill [4]. They reference the work of Gordon Allport, citing his conditions for optimal contact, specifically equal status; common goals; authority sanction; and no intergroup competition, as helpful but not necessary for the reduction of prejudice due to intergroup competition [1, 4].

Macro-scale desegregation is an essential condition for overcoming prejudice and developing an integrated society; however, it is not the only condition required. In *Eating Together Apart*, Clack, Dixon, and Tredoux (2005) explore how a city can be integrated in terms of racial distribution in housing and business, and yet individuals may still be experiencing 'parallel lives' in which micro-scale social boundaries prevent them from having meaningful interactions with members of different social or racial groups [2].

Much research on the issue of parallel lives and micro-scale segregation has been conducted in dining halls and school cafeterias. In a study of segregation in school cafeterias, Schofield and Sagar (1977) found by examining side-by-side and face-to-

face seating arrangements, that even a school which was relatively successful in achieving integrated enrollment still had significant micro-social segregation, a phenomenon that was particularly prominent among female students [6].

In the case of the University of Alabama, it has been 49 years since former Alabama governor George Wallace attempted to prevent black students from enrolling at the University of Alabama, and much has changed since then. Efforts have been made by the University of Alabama to promote diversity on campus. A diversity committee has been formed and charged to “promote and celebrate mutual understanding, dignity, respect, and cooperation among all ethnic, racial, religious, and social groups at The University of Alabama, and to actively discourage and prevent discriminatory practices toward any group” [8] Minority enrollment, while still low, has increased to 18% including 13% African American students, 3% Hispanic American, and 2% Asian American [7].

Much like the studies conducted by Clack, Dixon, and Tredoux in the U.K., Schofield and Sagan in the U.S., and by Rebekah Nathan in Arizona, we attempt to assess the degree of micro-social segregation by examining intergroup interactions in the context of a dining hall. Working in dining halls allows us to follow the methodological precedents of a number of different studies, and we believe that a dining hall provides a unique opportunity to observe interactions in a context which is used by a representative sample of the University of Alabama’s demographics, and which provides opportunities for interaction or self segregation where there are no formal racial boundaries.

Methods

For the purposes of our study, we decided to look at the individual as the unit of analysis rather than the group. We began by selecting three dining hallswas available for both afternoon and evening meals and located in different parts of campus. We attempted to select dining halls which would provide a representative sample of the campus population; however, it would be useful in a follow up study to gather data from every dining hall on campus. Over four months we collected four sets of data at each dining hall during both afternoon and evening mealtimes.

At each table we collected data for every individual present at the moment that we observed the group. For each individual we recorded the following nominal variables: Gender (Male = 0, Female = 1), White (No = 0, Yes = 1), Black (No = 0, Yes = 1), Other (No = 0, Yes = 1), a continuous variable for the

number of people at the table, and nominal variables for Male at Table (No = 0, Yes = 1), Female at Table (No = 0, Yes = 1), White at Table (No = 0, Yes = 1), Black at Table (No = 0, Yes = 1), Other at Table (No = 0, Yes = 1), Meal Time (Lunch = 0, Dinner = 1), and Dining Hall (1,2,3).

By collecting these data for each individual we were able to statistically analyze the demographics of those sitting in groups mixed by ethnicity, or by gender.

While establishing our inter-coder reliability, we encountered issues of racial and ethnic categorization. Because we were simply observing and not interviewing individuals, we could not allow them to self identify, so rather than attempting to identify various groups with a high degree of precision, we decided to group individuals as Black (representing individuals who appeared to be of predominantly African American decent), White (representing Caucasian individuals), and Other (representing individuals who did not obviously fit either of the former categories). Initially, we had discrepancies over the classification of individuals who appeared to be of evenly mixed decent; however we decided to default to a hypo-decent rule, meaning that anyone who appeared to be of mixed Caucasian and other, or of mixed Caucasian and African American would be classified according to their minority heritage.

Results

		Gender			
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	571	50.4	50.4	50.4
	female	561	49.6	49.6	100.0
Total		1132	100.0	100.0	

Our sample is fairly representative of the University population in terms of gender composition. According to the University of Alabama website, 54% of the student body is female, and 46% is male. Of our sample, 571 (50.4%) were male, and 561 (49.6%) were female.

Over the course of our study we collected data for 1132 individuals sitting in 487 groups. Of these individuals, 1008 (89%) were sitting in racially homogenous groups and only 124 (11%) were sitting in racially integrated groups.

		Integrated			
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.00	1008	89.0	89.0	89.0
	1.00	124	11.0	11.0	100.0
Total		1132	100.0	100.0	

Considering that the demographic breakdown of students is not even, we decided to calculate integration levels overall, as well as integration levels with respect to opportunities for integration. Since we observed 281 African American students and 851 non-African American students we decided to create a variable (OPP) representing the number of opportunities for integration. This variable assumes that a fair opportunity for integration consists of 1 African American and 1 non-African American sitting together at a table, therefore OPP = 281.

With respect to overall integration, which includes the number of African American and Caucasian students sitting at integrated tables, we would expect a maximum of 281 African Americans + 281 Caucasians or 562 (OPP x 2). Therefore, in terms of overall integration we see 124/562 or 22.1% of opportunities for integration being taken advantage of.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not white	362	32.0	32.0	32.0
	white	770	68.0	68.0	100.0
Total		1132	100.0	100.0	

Of our sample population, 770 (68%) were Caucasian, 281 (24.8%) were African American, and 81 (7.2%) were classified as other. According to the University of Alabama website, 82% of the student body is Caucasian, 13% of the student body is African American, and 5% of the student body falls into the category of other.

The percentage of African Americans in our sample was almost double that of the University of Alabama reported statistics, the percentage of students that fall within the category of “other” was substantially higher than that reported by UA, and the percentage of Caucasian students was substantially lower than that reported by UA. This means that our sample population was not a perfect representative sample of the student body; however, it is a close enough approximation of the demographics of the University of Alabama that we can still draw meaningful conclusions about racial interaction on campus which are not biased by a gross over- or under- representation of one specific demographic group.

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	9.812 ^a	1	.002		
Continuity Correction ^b	9.134	1	.003		
Likelihood Ratio	9.118	1	.003		
Fisher's Exact Test				.003	.002
Linear-by-Linear Association	9.803	1	.002		
N of Valid Cases	1132				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 30.78.
b. Computed only for a 2x2 table.

In 16.0% of cases, being African-American was associated with sitting in a racially integrated group, however, being Caucasian or Other was only associated with sitting in racially integrated groups in only 9.3% of cases (p=.002). When we calculated levels of racial integration for the racial categories Caucasian and “Other” separately, we did not find a significant difference in integration levels, so we decided to collapse them into one variable.

		inte2		Total	
		.00	1.00		
Black	not black	Count	772	79	851
		% within Black	90.7%	9.3%	100.0%
		% within inte2	76.6%	63.7%	75.2%
	black	Count	236	45	281
	% within Black	84.0%	16.0%	100.0%	
	% within inte2	23.4%	36.3%	24.8%	
Total	Count	1008	124	1132	
	% within Black	89.0%	11.0%	100.0%	
	% within inte2	100.0%	100.0%	100.0%	

When we calculated the levels of racial integration with respect to OPP, we found that 28.1% (79/281) of the time, being Caucasian was associated with sitting at a racially integrated table, and that 16.0% (45/281) of the time, being African American was associated with sitting at a racially integrated table.

		inte2		Total	
		.00	1.00		
Gender	male	Count	497	74	571
		% within Gender	87.0%	13.0%	100.0%
		% within inte2	49.3%	59.7%	50.4%
	female	Count	511	50	561
	% within Gender	91.1%	8.9%	100.0%	
	% within inte2	50.7%	40.3%	49.6%	
Total	Count	1008	124	1132	
	% within Gender	89.0%	11.0%	100.0%	
	% within inte2	100.0%	100.0%	100.0%	

When we calculated the levels of racial integration based upon the variable gender, we found that in 13.0% of cases, being male was associated with being in a racially integrated group, while, being female was only associated with being in a racially integrated group 8.9% of the time (P=.029).

When we calculated the levels of racial integration based upon the variable gender and with respect to OPP, we found that 26.3% (74/281) of the time, the variable Male was associated with sitting at a racially integrated table, and that 17.8% (50/281) of the time, the variable Female was associated with sit-

ting at a racially integrated table.

Discussion

The most interesting results of our analysis were the general trends (integration of men vs. integration of women; integration of African Americans vs. integration of non-African Americans) rather than the detailed specifics (integration of African American women vs. integration of Caucasian men). These results suggest that integration, defined here as interpersonal interactions taking place between individuals of distinct ethnic or racial backgrounds, is still extant at the University of Alabama. Only 11% of the total population sitting at tables which were integrated across racial lines. The levels of integration were slightly higher when calculated with respect to opportunities for integration, with 22.1% of opportunities for integration being taken advantage of. Our study also revealed that minorities students seem to utilize dining hall facilities at a disproportionate rate to the rest of the University of Alabama students.

The differential levels of cross racial interactions, 16.0% of African Americans sitting at integrated tables, and 9.3% of Caucasians sitting at integrated tables, can be explained to some degree by the number of opportunities for integration. For example, we would expect to see a higher percentage of African American students sitting at racially integrated tables than Caucasian and Other students, because there are roughly 3 times as many non-African Americans as African Americans in the dining halls. There were more opportunities for African American students to sit at racially integrated tables than there were for Caucasian and Other students. If the larger percentage of minority students sitting at racially integrated tables was the result of increased opportunities for racial integration relative to the majority students, then we would expect to see a higher actual number of majority students sitting at racially integrated tables in spite of their lower percentage.

This is reflected in our data, with 79 Caucasian or "Other" students sitting at racially integrated tables, and 45 African American students sitting at racially integrated tables. When we calculated the percentages of Caucasian and African American students sitting in racially integrated groups with respect to the number of opportunities they respectively had, we find that 26.3% of the opportunities to sit in racially integrated groups were taken advantage of by Caucasian students, but only 16.0% of the opportunities to sit in racially integrated groups were taken advantage of by African American students.

We believe that the lower percentage of Afri-

can American students taking advantage of opportunities for integration relative to Caucasian students can be explained through the idea of a cultural recovery period. Interacting with someone of a different cultural background may cause an increase in stress levels relative to interacting with someone of a similar cultural background. If this is the case, then it makes sense that a higher percentage of individuals in the minority position will take advantage of opportunities to interact cross culturally because they are immersed in the majority culture, but a higher actual number of individuals in the majority position will take advantage of opportunities to interact cross culturally because they are less likely to be stressed from previous cross cultural interactions. People in the majority position will have fewer opportunities to interact cross culturally, but because the majority of their interactions are low-stress, same-culture interactions, they will be more likely to take advantage of the few opportunities they have for cross cultural interaction. Members of the minority on the other hand, have more opportunities for cross cultural interaction, but may take advantage of those opportunities with less frequency because of their need to escape the stress of constant cross cultural interactions.

Most striking in this study was the disproportionate rate of females-to-males sitting at racially integrated tables. There were 74 males but only 50 females sitting in racially integrated groups. Males sat at integrated tables nearly 50% more often, which demonstrates the need for further study of the motivations of women for sitting, or not sitting, in racially integrated groups. It is possible that further work needs to be done specifically to promote racial integration among women.

Conclusions drawn from this study are partially limited by the difficulty of identifying and measuring true micro-social integration. Though people of two distinct racial groups are sitting in the same group at the same table, they may not interact in any meaningful way. Nevertheless, micro-scale interactions are a good indicator of racial integration. This study was further limited by our inability to ask individuals to self-identify their ethnic and racial backgrounds. It would be valuable to repeat the study with IRB approval to have individuals self-identify their ethnic or racial identities.

It would also be valuable to consider a follow-up study in which random students of the various racial groups represented in a given area were asked to monitor their own interactions and record how many interactions took place with members of their own racial group, and how many took place with members of other racial groups. This would be valuable in

helping us to understand if the low levels of racial integration that we observed were reflective of two distinct populations, those who engage in racially integrated interactions and those who do not, or if we are simply observing a frequency of interaction, meaning that the majority of students engaged in racially integrated interactions, but with a low frequency.

Conclusions

In conclusion, our study observed that levels of racial integration are still fairly low, and that further effort is needed to promote interracial interactions on campus. Examining integration on a macro-scale, such as the number of minority students on campus, or the number of minority students using specific facilities or resources, we see that the University of Alabama is making progress toward a more integrated student body. On a micro-scale, the University of Alabama has made some progress in promoting integration among students, but further work is needed. The rate of racial integration among women was disproportionately low compared to the rate among men, so further study and programs designed to promote integration among women would be valuable.

As discussed in the introduction, the key to promoting integration on campus is promoting activities which encourage students of differing racial backgrounds to work together towards common goals, on an equal standing, in a socially sanctioned context. Interactions consistently promote understanding, and therefore interactions across racial boundaries should be encouraged by the administration and the community.

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Preparation and Optimization of Electrochromic Devices

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Electrochromic devices (ECDs) undergo a reversible color change by means of a redox reaction that occurs when a voltage is applied. Applications of ECDs include windows, camera displays, and rear-view mirrors. In this project, ECDs were made using indium tin oxide (ITO) films as their electrodes because ITO is clear and highly conductive. The absorbances, resistances, and thicknesses of the devices as well as the time and voltage required to switch between states have been measured in order to optimize the device properties. The ideal ECD for our purposes would have the darkest film with the highest contrast ratio compared to the bleached state. The results of the optimization will allow for a comparison of devices made with commercial ITO to those made with ITO grown using pulsed laser deposition (PLD) in-house.

Introduction

Electrochromism is a property of certain materials that results in a reversible color change when a specific voltage is applied. This change occurs due to a redox reaction. It is not necessary to pass a continuous voltage because it retains the reduced state until an opposite voltage is applied. Some desirable characteristics of ECDs include fast switching times, high contrast ratios between states, and alterable colors because they allow the device to be more responsive and versatile [1].] Research is being done to tailor material properties to exploit them for various commercial uses.

One application of electrochromic materials is smart windows. According to the Department of Energy (DOE), about 30% of energy used to heat and cool buildings is wasted in those that use traditional windows [5]. This problem can be avoided by installing smart windows that allow for climate control and increased energy efficiency by affecting the solar energy entering buildings [7]. Lawrence Berkeley National Laboratory researchers estimate that using smart windows could eliminate more than 1% of the nation's annual energy usage, which would save roughly \$10 billion annually [5].

There are significant barriers to entry including expensive manufacturing processes, lifetime requirements, and lack of incentive [2]. However, green technologies are becoming more popular and companies such as SageGlass and Soladigm have begun entering the market. The former has done a few major window

installations at businesses and colleges and the latter will begin production once its factory is completed in 2012 [6, 8]. Their smart windows are programmable and can change based on various conditions or can be switched manually, similar to a thermostat. Besides electrochromic windows, there are other existing and potential markets for similar applications including rearview mirrors, sunroofs, windshield visors, privacy windows, cameras, camouflage materials, eyeglasses, and sunglasses [2, 4, 7].

Another potential application for electrochromic materials is in a sensor used to monitor the condition of frozen products. Bacteria flourish in warmer temperatures so keeping food properly frozen is important to avoid foodborne illnesses. The use-by-date printed on food packaging is determined under the assumption that the good was stored and transported under proper conditions. The electrochromic material would change colors based on temperature, thus allowing for identification of goods that have not been transported under proper conditions. For instance, if the packaging is warmer than the appropriate temperature, the electrode would become more conductive causing the sensor to change color, indicating that the food may be unsafe to consume [7]. The main hindrance to the development of this technology is tailoring the device to change color at the rate of deterioration of particular goods, but a simple prototype has already been developed [7].

Researchers are also trying to develop displays with paper-like appearance, texture, and visibility to appeal to the consumer who would like their display

to feel more natural. Electrochromic materials are good candidates for this application because they have a high reflective contrast ratio and can be easily constructed from a flexible plastic substrate to provide a paper-like texture. Those materials that can change from clear to three primary colors would be necessary for full-color displays. Prototypes have been developed but problems that have been encountered so far include stability and lifetime [3].

For this experiment, our design resembled the previously mentioned window applications because the substrate was clear. We used Poly (3,4-ethylenedioxythiophene)-poly (styrenesulfonate) (PEDOT) as the electrochromic film because its bleached and darkened states have high contrast, it is highly conductive, and it has a low redox potential [2]. The light blue PEDOT film spun is initially in the oxidized state. When 2.5 V is applied, the PEDOT accepts electrons, is reduced, and the film becomes a darker blue and mostly opaque. When the reverse voltage is applied, the film becomes a mostly transparent, light blue color. The transparency and opaqueness of the states depends on the thickness of PEDOT film. We used BMIM Cl as the liquid electrolyte. Since we used a liquid electrolyte instead of a solid one, the bleaching and darkening process occurs over a few seconds instead of a few minutes [2]. The purpose of this study was to optimize parameters of the ECD prototypes that would result in the greatest contrast ratio between the bleached and darkened states.

Experimental

Film Characterization

Glass substrates were masked (2 cm × 2 cm), and 1, 3, 6, and 9 layers of PEDOT were spun at 2000 rpm using a spinner. After spinning each layer, the film was baked at 100°C on a hot plate for 5 minutes and then for 20 minutes after the final layer. Spinning these films was necessary in order to characterize the PEDOT films without interference from the ITO. Surface resistances were taken using the standard two-probe method. Thicknesses of the PEDOT films on glass were measured using the profilometer and the absorbances were obtained using a Cary 300C UV/Vis spectrophotometer. The absorbances were measured at the wavelength 244 nm and results reported are averaged results from five measurements.

Device Fabrication and Characterization

Commercial ITO on glass substrate was obtained and two thin strips of ITO were etched using 5M HCl. Then, the four substrates were masked (2 cm × 1.5 cm), and 1, 3, 6, and 9 layers of PEDOT were

spin coated at 2000 rpm. After spinning each layer, the film was baked at 100°C on a hot plate for 5 minutes, and for 20 minutes after the final layer. Etching the ITO was necessary to compare the PEDOT films to the previous PEDOT films on glass in order to verify that the films had similar characteristics without interference from the ITO. Surface resistances were taken using the standard two-probe method. The probes were placed on the part of the film where the ITO was etched. The absorbances of the PEDOT films on ITO in their neutral state were measured by manually subtracting the ITO and glass contribution. The absorbances of the PEDOT on ITO were then compared to the absorbances to those from the PEDOT on glass only. ECDs with 3, 6, and 9 layers of PEDOT were prepared by sandwiching 1 mL of the ionic liquid electrolyte, 1-butyl, 3-methylimidazolium chloride ([BMIM]Cl), between ITO with PEDOT and ITO without PEDOT as shown in Figure 1. The layers were staggered so that the electrodes were accessible for testing. A device with 1 layer of PEDOT was not made because the neutral state of the film was hardly evident and its absorbance was so low that it returned negative values after subtracting the glass' contribution.



Figure 1: A side view of the ECD displaying the positioning of the four components.

Device Testing

After constructing the ECDs, a voltage range of 2.4 V to 2.8 V at a speed of 0.5 V/s was applied using the linear sweep setting of the Electrochemical Workstation causing the ECDs to darken. The films bleached when the range of -1.9 V to -2.4 V was applied at the same speed. A range was used instead of a particular voltage to ensure that the films completely changed states. The absorbances after darkening and after bleaching the films were taken and compared also by manually subtracting the ITO and glass contribution.

Results and Discussion

Characterizing the PEDOT film on glass confirmed that absorbance of the neutral state is linearly related to the thickness of the film. The graph had a high R^2 value of .9482, meaning the relationship could be used to predict the absorbances of various thicknesses to a fairly accurate degree (Figure 2). A com-

parison between the absorbance of the PEDOT on the glass to the PEDOT on the ITO was attempted in order to verify that the films had the same thicknesses. However, since ITO and glass absorb between 200 and 300 nm and the absorbances for the PEDOT on glass films was taken at 244 nm, the results were inconclusive. A comparison was also made between the thickness and resistance of the film, which demonstrated that as the thickness increases, the resistance decreases exponentially (Figure 2). The resistance of film on the etched area also displayed a similar correlation (Table 1). However the PEDOT on ITO has lower valued of resistance than the PEDOT on glass because each film had slightly thicker edges (edge beads) due to the accumulation of PEDOT during the spin coating process. Therefore, the resistance measurement had to be taken on the edge where the ITO was etched resulting in resistances that are lower than films solely on glass.

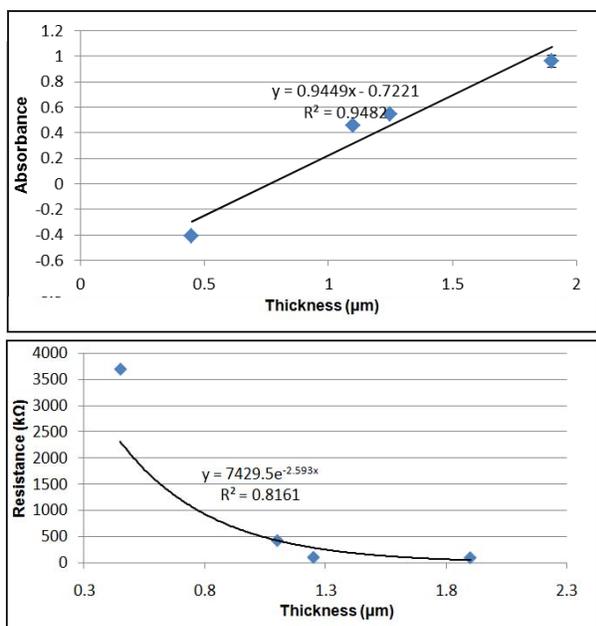


Figure 2: Verification of the linear relationship between thickness and absorbance. Absorbance was measured at 244nm where the maximum absorbance occurred for most of the films (top). Graph displaying that the film resistance exponentially decreases as the thickness increases (bottom).

The plot comparing the absorbance of the bleached and darkened state for the ECD with 3 layers of PEDOT is displayed in Figure 3. The maximum percent difference in absorbance was 46.5% at 624 nm. The plot for the ECD with 6 layers of PEDOT is

Number of Layers	Resistance of PEDOT on Glass (kΩ)	Resistance of PEDOT on Etched ITO (kΩ)
1	3690	3220
3	425	417
6	103.6	62.6
9	95.4	41.7

Table 1: Resistance comparison between PEDOT on glass and PEDOT on etched portion of ITO. The resistances show a similar exponentially decreasing trend as the thickness of the film decreases, but the resistances of the PEDOT on etched portion is lower than the PEDOT on glass due to the edge bead.

displayed in Figure 4. The maximum percent difference in absorbance was 83.2% at 623 nm. The plot for the ECD with 9 layers of PEDOT is displayed in Figure 5. The percent difference in absorbance was 32.2% at 623 nm. The 9 layer device was not as stable as the 3 and 6 layer devices and only bleached slightly in one corner of the film. One possible reason that the device failed to completely change states could be that the film was too thick for the anions to leave the surface and complete the redox reactions. The corner that was able to bleach slightly may have been thinner than the rest of the film, thus enabling it to bleach. Note that the edge of the film did not bleach, most likely because the film is even thicker on the edge bead. The camera used was unable to capture this slight bleaching, so pictures of the 9 layer device are not included.

Since this experiment is most applicable to the smart window application, the contrast ratio between states is the most important factor because it either allows or restricts light to pass through the window. Based on maximum percent difference between the bleached and darkened states, the optimal number of layers of PEDOT was 6 layers. Although the 9 layer device was unable to successfully bleach, it did have the highest absorbance of the three devices which may be useful for other applications, but is not ideal for ECD applications.

The time to switch states is also significant for applications. The ECDs took about 5–6 s to darken and about 3–4 s to bleach. This is consistent with previous reports that bleaching takes less time than darkening [2]. The time to switch states did not vary significantly based on the number of layers, possibly because the surface area being tested was small (3 cm²) and time differences would be nominal. In order to test switching times for ECDs with varying number

of layers of PEDOT, it would be necessary to test a larger surface area to make the time differences discernible.

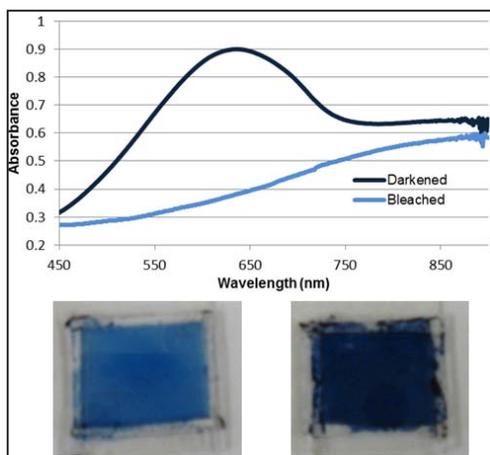


Figure 4: Comparison of the darkened and bleached states of the 6 layer PEDOT ECD in the visible range (top). The maximum percent difference in absorbance is 83.2% at 623 nm. Images of bleached (bottom-left) and darkened (bottom-right) 6 layer PEDOT ECD.

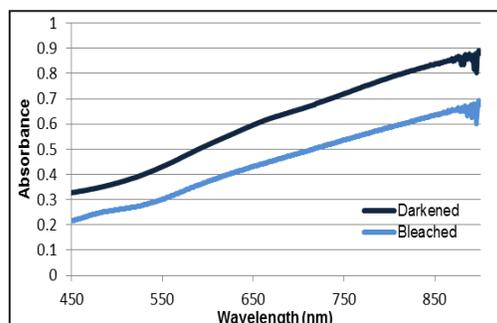


Figure 5. Comparison of the darkened and bleached states of the 9 layer PEDOT ECD in the visible range. The maximum percent difference in absorbance is 32.2% at 623 nm. Images are not shown because there were no visible differences to present.

Conclusion

This experiment focused on optimizing parameters for transparent applications of ECDs such as smart windows. The ideal device would have the darkest film with the highest contrast ratio compared to the bleached state, which would be useful to control how much light can pass through the window. The results

demonstrated that the optimal number of PEDOT layers is 6 based on the maximum percent difference in absorbance. The 9 layer device may have been unable to successfully change states because the film was too thick for the anions to leave the surface. This finding suggests that there is a limit to the amount of light this type of device is able to absorb while still retaining the ability to bleach, which could limit the applications. Using the optimal number of layers, a comparison can be made between ECDs made with commercial ITO to those made with in-house ITO in future experiments.

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Environmentally Responsive Drug Release Matrix

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Controlled medicinal drug delivery remains a research focus within public health in order to enhance patient compliance with their medications, drug efficiency, and the reduction of side effects of drugs. Pectin, an edible plant polysaccharide, has is useful for the construction of drug delivery systems for specific drugs. The solubilities of several derivations of esterified pectin have been tested in a pseudo-gastric environment, as well as in a pseudo-intestinal solution, in order to determine their ability to dissolve in the human body. Studies in this project demonstrate the flexibility and usefulness of pectin as a means for drug delivery.

Introduction:

Pectin is a polysaccharide extracted from the cell walls of citrus fruits and is used commercially as a gelling agent, a thickening agent, and a food stabilizer [7,9]. There are two common forms of pectin: High methoxy ester pectin (HMP; Fig. 1) and Low methoxy ester pectin (LMP; Fig. 2). These polysaccharides can be used to encapsulate chemicals for drug delivery. Encapsulated drug delivery can be used to deliver potentially dangerous compounds to areas of disease and uncontrolled cell division within the human body. In an effort to regulate the release of the encapsulated drugs the different pectin samples were functionalized and tested for dissolution in various pH solutions.

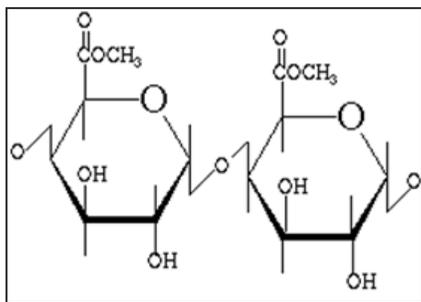


Figure 1: Structure of HM Pectin

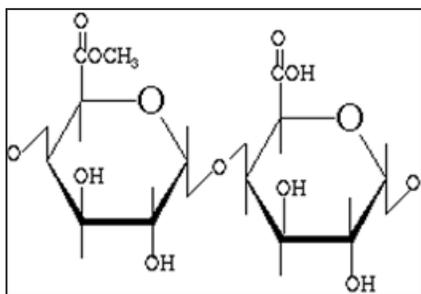


Figure 2: Structure of LM Pectin

Pectin Synthesis for Commercial use

In producing pectin for commercial use, a pectin factory will first receive apple residue (pomace) or citrus peel from a number of juice producers. In most cases this material has been washed and dried so it can be transported and stored without spoilage. The raw material is added to hot water containing a processing aid (usually a mineral acid, although others such as enzymes could be used). After time has allowed for the extraction of pectin, the remaining solids are separated, by filter, centrifuge, or other means, and the solution is clarified and concentrated by removing some of the water. Either directly, or after some further holding time to modify the pectin, the concentrated liquid is mixed with an alcohol to precipitate the pectin. The precipitate is separated, washed with more alcohol to remove impurities, and dried. The alcohol wash may contain salts or alkalis to convert the pectin to a partial salt form (sodium, potassium, calcium, and ammonium). Before or after drying, the pectin may be treated with ammonia to produce amidated pectin if required. The dry solid is ground to a powder, tested, and blended with sugar or dextrose to a standard gelling power or other functional property such as viscosity or stabilizing power [7, 9, 13].

Salicylic Acid (SA)

Salicylic acid is a crystallized molecule that is modified to create a variety of products like, aspirin, acne cream, dye, flavoring, toothpaste, and food preservatives. Salicylic acid also operates as a major plant defense hormone. The molecular structure for salicylic acid is, $C_6H_4(OH)CO_2H$. Salicylic acid functions as a carboxylic acid as well as phenol. A carboxylic acid is an organic carbon functional group, characterized by the presence of a carboxyl group. A phe-

nol is another organic compound; comprised of an aromatic cyclo-hexagonal ring, with a hydroxyl group bonded directly to it. In salicylic acid, the hydroxyl group is connected alongside the carboxyl group [2]. Salicylic acid is slightly soluble in water, but is totally soluble in ethanol and ether. It is economically prepared from sodium salicylate, which is derived from sodium phenoxide and carbon dioxide at high pressure and temperature in a Kolbe-Schmitt reaction. Sodium salicylate is then reduced to yield the desired salicylic acid. To produce aspirin, salicylic acid is acetylated using acetic anhydride, yielding aspirin and acetic acid as a byproduct. By using a process involving the esterification of the phenolic hydroxyl group of salicylic acid, the derived product still retains some of its potency as a pain killer while reducing its acidity [3].

Experimental Procedure

Pectin Solubility test: A quantity of ~100 mg of non-modified or modified pectin and was weighed and recorded, then added to 10 ml of a particular solvent in a 50 ml beaker covered with Parafilm and shaken for 24 hrs on an orbital shaker. The solution was filtered through Whatman filter paper No. 41 and the paper is re-weighed after complete drying.

Preparation of pH solutions: Two pH solutions, 1.2 and 7.4 were used to mimic the gastric and intestinal environments of the human body. To make the pH 1.2 buffer 425 mL of 0.2 M HCl was added with 250 mL of 0.2 M KCl, and 325 mL of Deionized (D.I.) water. To create the pH 7.4 buffer, add 160.4 mL of 1 M K_2HPO_4 to 19.8 mL of 1 M KH_2PO_4 , then dilute the combined 1 M solution to 1 liter with D.I. water.

Pectin Functionalization: Functionalization is the addition of a functional group to a molecule, in this case, pectin. For example, making Salicylic Acid functionalized pectin, requires HMP (High Methoxine pectin), Salicylic acid, P-toluenesulfonic acid and DMF (Dimethylformamide) to be mixed together at 60° Celsius, in the presence of Nitrogen gas for at least 24 hours. After mixing is complete, the solution is filtered out of the liquid solvent and the remaining precipitate represents the functionalized pectin. Functionalization of pectin allows changes in the physical properties of the pectin, including solubility in water and melting points. More importantly for this experiment, functionalization alters the rate of dissolution of pectin in aqueous solutions.

Spray drying the Pectin: To test the functionalized pectin it must first be in a dehydrated state. (Figure 4) This state is achieved by a spray dry technique known as micro-encapsulation. To spray dry the



Figure 3: Drug Release Apparatus. The drug release apparatus is comprised of a vortex and magnetic stirrer. It is used to stir the functionalized pectin in the aqueous solutions during the release studies.

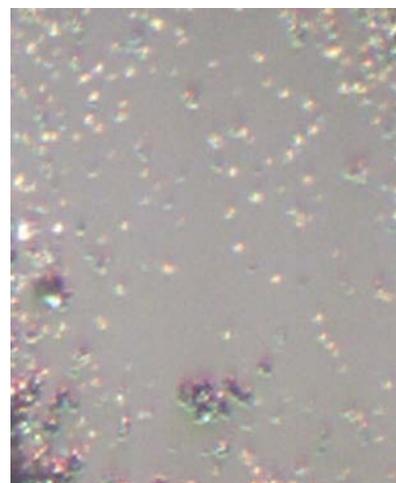


Figure 4: Pectin beads after being spray dried

functionalized pectin in this experiment, the Büchi Mini Spray Dryer B-290 was used to spray dry the functionalized pectin. The settings for the spray dryer are as follows: inlet temperature set to 150° C, outlet temperature set to 50° C, aspirator (air flow) set to 100%, rotameter (for air quantity) set to 40, and nozzle cleaner set to 40 as well. Once the solution is done spray drying, the now dehydrated functionalized pectin can be tested in the release studies.

Salicylic Acid Release Studies/MSA: Each pectin sample contained 10% salicylic acid, and was weighed to approximately 0.2 grams, then placed in the drug release basket apparatus (Fig. 3). The basket with pectin beads (Fig. 4) was lowered into the pH solution and left to spin for 24 hrs. The UV-Visible

Spectrophotometer recorded the absorbance at 296 nm, which is the wavelength of light absorbed by salicylic acid. After the 24 hour run, the solution, containing the dissolved pectin underwent method of standard additions (MSA) to determine the concentration of a salicylic acid released from the pectin beads. For the initial MSA, a small amount of the solution was placed into a quartz glass cuvette, and scanned from 200 nm to 400 nm with the UV-Visible Spectrophotometer. The MSA calibration curve was measured by spiking the sample with 250 μ L of standard solution (100 mg/L salicylic acid), then scanned. The sample was spiked with another 250 μ L and scanned again, followed by a third spike of 250 μ L and scanned the final time.

Data

Upon completion of this experiment it was determined that all of the pectin samples totally dissolved to form a homogenous mixture with each basic solution (pH of 7.4) but failed to totally dissolve in the acidic solution (pH of 1.2.). From this data, it is observed that the functionalized pectin has a much lower solubility in acidic solutions, while having a very high dissolution rate in neutral/basic solutions. These results demonstrate that functionalized pectin can be used as an alternative for drug delivery through the stomach and into more “basic” areas of the gastrointestinal system, like the intestines.

Future Work

In the future, different esterified pectins will be created and tested, in order to compile more data for this study. It is critical to determine how each pectin available will react when dissolved in each buffer solution.

Sample	Solubility (g/mL)	Total time to reach the saturation (hours)
HMP (DE= 71.5 %),	0.0106 \pm .003	24 hrs
LMP (DE = 9.9%)	.0126 \pm .0057	24 hrs
C12 Pectin	.0089 \pm .0009	24 hrs
Amidated LMP (DE=26 %, Degree of amidation= 22%)	.0133 \pm .0053	24 hrs

Table 2: Results from the solubility tests for the non-functionalized pectin.

Pectin	Drug content (%)	Mean bead diameter (μ m)	Percentage salicylic acid released in dissolution media											
			HCl buffer ~ pH 1.2				Distilled water				Phosphate buffer ~ pH 7.4			
			T ₃₀	T ₉₀	T ₁₅₀	T ₁₄₄₀	T ₃₀	T ₉₀	T ₁₅₀	T ₁₄₄₀	T ₃₀	T ₉₀	T ₁₅₀	T ₁₄₄₀
HMP	7.6	4.2	11	27	36	53	27	49	64	97	17	41	55	80
LM-104	8.6	4.5	4	9	14	19	31	55	65	75	10	24	31	42

Table 3: Results from the release studies. Only the HM and LM-104 functionalized pectins are shown in the table below.

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Spontaneous Imitation in Children with Autism Spectrum Disorders

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The ability to spontaneously imitate other people has been linked to the development of language, engagement in symbolic play, and the learning of social mores of a society [18, 10]. This spontaneous initiation of motor actions has been found to be impaired in children with autism [10, 15]. Little research has examined the ability to spontaneously imitate verbal actions in children with autism. The current study examined spontaneous object and vocal imitation in children with autism spectrum disorder (ASD) in comparison to a typically developing (TD) control group using Ingersoll's Unstructured Imitation Assessment [10]. In the current study, each child was given ten opportunities to imitate vocal and physical actions of another. Results suggest that TD participants verbally and behaviorally imitated the experimenter more often than ASD participants, demonstrating that social imitation is impaired in ASD preschoolers. The development of ASD therapies which focus on improving social imitation may improve therapeutic results.

Introduction

Autism spectrum disorders (ASD) are pervasive developmental disorders characterized by delays in the development of socialization and communication skills, and include Asperger's Syndrome and Pervasive Developmental Disorder- Not Otherwise Specified. These symptoms typically begin in infancy and persist across the lifespan. ASD is a neurological disorder with an onset before three years of age and is characterized by impairments in the development of communication skills, reciprocal social skills, language, and the presence of restricted behaviors and interests [1]. However, the presentation of these symptoms may change throughout the course of development and the nature of symptoms vary from child to child [19]. The Centers for Disease Control [4] estimates that the prevalence of autism is 1 in every 110 births in the United States.

Imitation is important for understanding ASD as deficits in imitation play a significant role in the characteristic social and learning deficits in the disorder [24]. In particular, imitation deficits associated with ASD affect one's ability to learn the social aspects of human cognition such as social responsivity and reciprocity, understanding another's intentions, language, and the development of new behaviors [24, 15, 16]. Therefore, it has been proposed by numerous researchers that imitation is an essential developmental skill that should be targeted by early intervention for the improvement of other necessary social skills.

The purpose of this study was to examine how motor and verbal imitation may correlate with children's overall developmental level and symptoms of ASD.

The Importance of Imitation

Imitation is defined as "behavior displays in which one individual voluntarily reproduces behavior as observed in another who acts as the model for the form of a behavior" [2]. However, it is important to note that motivation, cognitive abilities, and executive functions could all contribute to why an individual may choose to imitate [18]. Further, imitation serves a variety of purposes, including learning functions and social functions. Imitation is a fundamental skill required to learn language, how to interact in social relationships, and the development of cognitive skills such as symbolic thinking and manipulating tools.

The research on imitation has focused on the importance of learning through imitation. Learning through watching and imitating others is an advantage for young children as they learn how to use and control objects [16, 20]. According to Nadel [18], the "golden age" of imitation occurs between 18 and 42 months of age in typical development. This is when the two functions of imitation, learning and nonverbal communication, begin to be used to learn motor strategies and language.

Motor Imitation in Typical Development and Autism

Motor imitation in individuals with autism has been of significant interest since Ritvo and Provenca [24] reported significant motor imitation impairments in children with autism.

Compared to children with typical development, children with ASD perform significantly better on tasks which involve imitation of actions on objects as opposed to imitation of body and facial movements [3]. It has been found that children with ASD perform better on imitation tasks that are meaningful (i.e. imitating brushing another's hair) over nonmeaningful (i.e. imitating walking a brush across a table) [3].

Stone, Ousley, and Littleford [27] compared how children with ASD, with other developmental delays, and with typical development imitate body actions and actions with objects. Results indicated that as children with autism developed from age 2 to age 3, imitation of body movements and single step actions on objects improved, suggesting the possibility that single-step actions were delayed in autism. This study also showed body and object imitation are two different domains as both typically developing children and children with ASD performed better on imitation of body movements than actions with objects.

Zachor, Ilanit, and Itzhak [29] conducted a study that examined the performances on motor imitation tasks by children with autism. Results indicated that performance was not linked to the child's autism severity or motor abilities, but rather to socio-communication deficits. Furthermore, Zachor and colleagues [29] reported that cognitive level, motor development, experience with social-reciprocal interactions, and responsiveness deficits are the most important underlying mechanisms in motor imitation skills. They also found that fine motor skills were positively correlated with imitation on actions with objects. Interestingly, the participants with poor fine motor abilities performed better on the tasks involving body gestures. Based on these conclusions, individuals with ASD will traditionally perform worse on tasks of imitation; however, as these individuals age their skill sets may be improved due to imitation specific intervention and therapies.

Hobson and Hobson [8] conducted a study examining imitation in the context of goal-directed tasks and style. They measured separately whether children imitated a fundamental action and whether they did it with similar style of movements. Hobson and Hobson [8] found that children with autism perform well in relation to imitating actions but showed greater deficits in relation to the processes which re-

quire a social or "subjunctive interaction with others" (p. 176).

Language Development and Imitation in Typical Development and Autism

The majority of research on imitation has examined motor imitation; thus, minimal attention has been paid to vocal imitation. Between the ages of 2-6 months, infants are actively responding to and initiating vocal communication and will begin spontaneously imitating or will mirror their mothers' expression [13]. This type of communication allows infants to develop self-other awareness as well as build the foundations of social relationships through exposure to emotions and shared experiences [25].

Language in individuals with autism is usually delayed with the average age for first words being 38 months in contrast to 8-14 months of age in typically developing children [5, 9]. It is estimated that up to 25% of individuals with ASD will remain non-verbal [28]. Language of individuals with ASD may also be characterized by the use of echolalia, a form of vocal imitation [21, 22]; the rote use of language or scripted language [6]; and pronoun reversal [14, 6]. Current research on echolalia is moving away from theories which postulated that the presence of echolalia was in and of itself a communicative disorder and its function detrimental to the development and use of complex language [21]. However, beginning with research conducted by Prizant, the categorization of echolalia has changed dramatically and research is examining its functions as a coping mechanism and as a learning tool, and its use to guide individuals through various tasks [21].

Both motor and verbal imitation may be divided into two broad categories: elicited imitation and spontaneous imitation. Elicited imitation refers to the explicit instructions to repeat an observed action or observed vocalization, whereas spontaneous imitation refers to the more automatic repeating of observed actions or verbalizations. Spontaneous imitation may be related to the development of such tasks as language and social interaction [7, 26].

Nadel [18] conducted a study to measure the ability to spontaneously imitate motor actions and to imitate when instructed to do so. It was found that spontaneous imitation was related to their developmental level, their motives, and familiarity with the actions. Nadel [18] concluded that spontaneous imitation and elicited imitation were not correlated with one another. Furthermore, children with autism appear to be more discriminatory in the spontaneous actions they choose to imitate, such as not spontaneously imi-

tating nonmeaningful gestures (i.e., walking a brush across a table) [18]. The results of Carpenter's research [3] revealed that it is the "shared, social aspects of imitation [that] are most affected in children with autism" (p.52). Yet, in a spontaneous imitative context, individuals must understand what the intentions and goals of another individual are in order to successfully replicate actions.

The Current Study

Although extensive research has been conducted concerning motor imitation, there has been very little concerning language imitation. Many of the motor imitation tasks that have been developed have included a language component with the task even though they emphasized the motor aspects. Language imitation has historically received less attention in comparison to motor imitation. Further, the majority of previous studies of motor imitation have examined elicited, rather than spontaneous, imitation skills. This study addressed the current gap by directly comparing spontaneous motor and spontaneous verbal imitation.

The current study examined the relation between object and vocal imitation in typically developing preschoolers and preschoolers who have ASD. The experimental task for this study examined spontaneous imitation in a naturalistic play setting developed by Ingersoll [11]. During the study the examiner modeled motor and verbal actions using a set of toys, while a second, exact set was freely available to the child in order to provide the opportunity to spontaneously imitate motor and verbal actions.

Methods

The purpose of this study was to examine the relationship between language imitation and imitation of motor actions on objects in a spontaneous, socio-interactive context in preschool aged children with an autism spectrum disorder (ASD) and typical development. The task was based on Ingersoll's Unstructured Imitation Assessment [11].

Participants

Two groups of children were recruited as part of a larger study that examined the differences in imitation abilities between typically developing children and children with ASD conducted at the University of Alabama. Thirty-one children participated in this experiment with 16 ASD and 15 TD participants. The mean chronological age was 3 years 8 months (3;8), with the youngest child being 2;0 and the oldest child

being 5;8. The mean age for the ASD participants was 4;2, and the mean age for the TD participants was 3;1. The TD and ASD groups were matched on mental age based on scores from the Mullen Scales of Early Learning.

Measures

Mullen Scales of Early Learning [17]. The Mullen assesses cognitive development through 5 measures: gross motor, fine motor, visual reception, receptive language, and expressive language. The gross motor subscale was not administered for this study. The last four measures, which are categorized as "cognitive" skills, are summarized into an Early Learning Composite (ELC) score. The Mullen was used to obtain an overall developmental level and receptive language mental age for each child for the purposes of matching the groups. The Mullen can be administered to children between the ages of 0-68 months. The time required for administration is dependent upon the age of the child and therefore may require between 15 to 60 minutes. Furthermore, as the age of the child increases so does the raw score of the child, which is evidence of good construct validity of the Mullen. Also, the Mullen has been found to have stronger correlations to assessment instruments that measure similar dimensions such as cognitive, language, and motor development than those that measure different scales. The internal-consistency reliability composite score is .91 and test-retest reliability for cognitive scales median is .84 (1-24) months and .76 (25-56 months)

Unstructured Imitation Task [11] The task of this study was a measure created by Ingersoll (2010). In the task ten actions are accompanied by ten verbal markers. Two identical sets of toys were present in the room during the experiment; one set was used by the examiner to model motor and verbal actions, and the second set was freely available to provide an opportunity for the child to spontaneously imitate motor and verbal actions. The examiner did not provide explicit instructions to imitate during the session.

Warm-up phase. The first phase of the procedure occurred for the duration of two minutes. Throughout the study the child was free to engage in any action and play with the toys in any manner they wanted. During this warm-up phase the experimenter imitated all of the child's verbal and non-verbal actions but the experimenter did not model any new actions.

Modeling Routine. The second phase of the procedure was marked by the verbal cue of “Watch me” in order to engage the child’s attention. New actions were modeled on an average of one per minute. Each action was modeled three times in a row every five seconds. Actions were modeled with toys that the child was not currently holding. Actions could be modeled in any order but once the action had been modeled the experimenter did not repeat the action again. During the task no praise was provided for correct imitation. Social smiles were used but were not contingent upon whether or not the child imitated the action/verbal marker. Modeling continued until each of the ten actions and associated verbalizations had been modeled or until the child became frustrated or asked to quit.

After the experimenter modeled a motor action and verbalization three times and gave the child an opportunity to respond, a 45 second break occurred before the next action and verbalization were modeled. During the 45 seconds, the experimenter imitated the child’s actions and narrated the child’s play. The child’s statements (but not other forms of verbalizations) were imitated during this 45 second break. After the break, the examiner modeled the next action and verbalization.

Results

Coding

In this study the imitation of actions on objects and imitation of language was scored as two separate measures through a coding system. Across both types of imitation, a score of “0” signified no attempt or an incorrect response, a score of “1” signified an attempt by the participant to imitate the actions or language of the experimenter, and a score of “2” signified a complete imitation by the participant as performed by the examiner. The coding method of imitation of actions on objects was adapted from the Unstructured Imitation Scale- Object by Ingersoll (2010). In order to establish inter-rater reliability, inter-rater agreement was based on 20% of the collected data with an agreement of 90% between coders. Disagreements were resolved by consensus and review of sessions through video recordings.

Action

A Chi Square Test of Independence was used to analyze the differences between the typically developing (TD) and the autism (ASD) groups for each trial of action repetitions. No significant differences were

found between the TD and the ASD groups, $\chi^2(2) = .90, p = .64$, though the results suggest that TD participants imitated actions more than the ASD participants did. See Figure 1.

Verbal

A Chi Square Test of Independence was used to analyze the differences between the typically developing (TD) and the autism (ASD) groups for each trial of verbal repetitions. No significant differences were found between the TD and the ASD groups, $\chi^2(2) = 2.06, p = .36$, though the results suggest that TD participants imitated vocalizations more than the ASD participants did. See Figure 1.

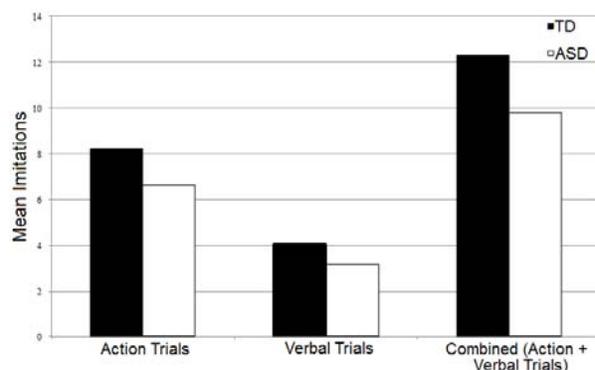


Figure 1: Mean action and verbal imitations for typically developing (white) and ASD participants (dark) across ten trials (action, verbal, and combined in the figure)

Discussion

The purpose of this study was to compare the imitation of children with Autism Spectrum Disorders (ASD) and typically developing children (TD) in their ability to spontaneously imitate verbal and motor actions. Due to the significance of spontaneous imitation in the development of language and its importance in the learning of the social rules within a society (Nadel, 2002; Ingersoll, 2008), spontaneous imitation is an important aspect of developing a repertoire of social behavior and in cognitive development. However, to date there has been little research exploring this ability in children with ASD and its relation to impaired social interactions.

The methods used in this study were based on a study by Ingersoll (2010) which examined the outcome of spontaneous imitation training (reciprocal imitation training) in participants with ASD. Researchers in this study used a template based on the Unstructured Imitation Assessment (UIA; adapted from Ingersoll, 2010) of ten actions that were paired

with ten verbal imitations. In contrast, Ingersoll recruited 21 children with ASD between the ages of 27 and 47 months who were then matched on expressive language and then randomly assigned to the treatment group (Reciprocal Imitation Training) or the control group (participants received no intervention through the study and continued any pre-existing services or treatment within the community prior to their inclusion in the study).

Although the results of this study suggest that TD participants imitate verbally and behaviorally more than ASD participants did, the differences between the groups of children were not significant and therefore do not corroborate the results found in Ingersoll's study or previous studies which examined spontaneous imitation in preschool participants with ASD and typically developing participants. One explanation is the age discrepancies between the participants in the two studies. The participants within the Ingersoll study (2010) were on average 41.36 months within treatment group and 37.20 months within the control group and therefore younger on average than those recruited to participate in this study. During data collection, researchers found that older and typically developing participants would attend to the examiner during the task but preferred and encouraged the examiner to engage in symbolic or pretend play rather than the verbal and behavior imitations, whereas the younger participants with ASD were uninterested in the examiner's attempts to engage them in social play and preferred to be allowed to engage in play on their own and did not seek social gratification from the examiner.

This study differs from the Ingersoll study due to the fact that language was coded as a separate measure within this study and examined as a separate dimension between the ASD and TD participants. This study also adds to the literature of language and its relation to spontaneous (social) imitation within the ASD population. As discussed in the results, the ASD group imitated the examiner less often than the TD group in both the verbal and imitation of actions on objects conditions, supporting previous research concerning the performance of children with ASD in relation to spontaneous imitation. Due to the growing literature on the nature of social imitation deficits within the ASD community, this instrumental skill is an area of great importance in development and therefore an area to be addressed in future research and in therapy.

Possible implications of this study include an addition to the literature concerning verbal imitation and the topic of spontaneous (social) imitation in ASD populations. As previously discussed, the develop-

ment of spontaneous imitation and thereby social, language, and cognitive skills are instrumental in development; therefore, methods and intervention strategies for the development of these skills appear to be of great benefit to children with ASD as the research supports impaired capabilities within this domain. Furthermore, this study may serve as a platform in conjunction with previous studies concerning imitation in order to explore the possibilities of intervention within the developmentally diverse ASD population.

Author Note

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Reviews

An Introductory Review of the Role of Synaptic Plasticity in Memory

Grant Fairchild

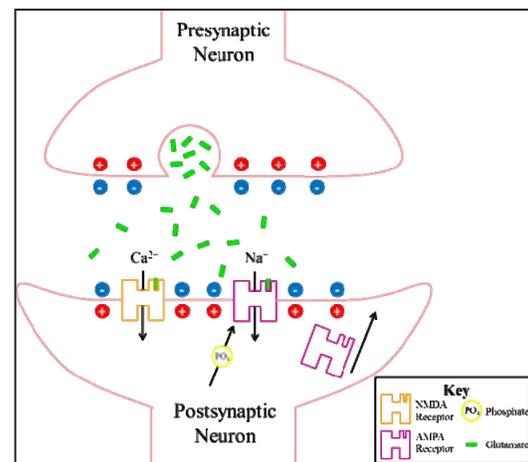
Memories have a physical basis in the intricate neuronal networks of the brain where information is represented as electrical signals propagating through neuronal circuitry. The flow of information is determined by the synaptic connections between neurons and by the relative influence presynaptic neurons have over the postsynaptic neurons that they connect to. The influence that presynaptic neurons have over postsynaptic neurons is determined by the previous success of their synapses in contributing to the firing of action potentials in the postsynaptic neurons. This selective adaptivity of synapses is known as synaptic plasticity. The cellular and molecular mechanisms of synaptic plasticity are vital to an animal's ability to learn and remember information. Without a few crucial proteins, it is likely that the formation of memories would be unattainable.

Introduction

In the 1940s, neuropsychologist Donald Hebb hypothesized that learned information could be stored temporarily in a network of neurons in the form of a reverberation of neuronal firing of action potentials and that this reverberation strengthened the synapses of the cells participating in it [1]. He called the active circuit of neurons a “cell assembly” and the reverberation a “trace” [1]. The trace would serve as the neural correlate of working memory [1,2]. He thought that this trace would induce a physiological change in the synapses (specifically, Hebb hypothesized that synaptic surface area would increase) that added to the stability of the association between the neurons in the cell assembly [1]. Summarized by Carla Shatz of Stanford University, “Cells that fire together, wire together” [3]. The strengthening of synapses of cells that fire together is known as long-term potentiation (LTP) [4]. Although Hebb’s idea has been added to and modified, research since his time has shown that his hypothesis was quite accurate. One corollary to his hypothesis is that the synapses of cells that fire in an unsynchronized manner become weakened; this is known as long-term depression (LTD) [4]. LTP and LTD taken together constitute the BCM theory (named after the scientists that added the corollary regarding LTD, Bienenstock, Cooper, and Munroe) and are the predominant forms of synaptic plasticity [5]. As information is thought to be physically manifested in the connections between neurons, synaptic plasticity is thought to be necessary for the for-

mation of memories [6,7].

When considering neuronal circuitry, it is important to keep in mind that an action potential in a postsynaptic neuron is not triggered simply by an action potential fired by a single presynaptic neuron.



Rather, a great many presynaptic neurons synapse on the postsynaptic cell, and action potentials from each of them depolarize the cell a little bit. If enough of them fire at once, they will collectively depolarize the postsynaptic cell to an extent sufficient to trigger within it an action potential which the cell will then pass on to many other neurons. The crux of BCM theory is that when a presynaptic neuron successfully contributes to this postsynaptic action potential, its synapse with the postsynaptic cell will strengthen, but when a presynaptic cell fires without enough other presynaptic cells firing to cause a postsynaptic action potential, its synapse with the postsynaptic cell will weaken [5].

Molecular Mechanisms of Synaptic Plasticity

The N-methyl-D-aspartate receptor (NMDA receptor) is a remarkable protein that is the linchpin of synaptic plasticity. It is a membrane-bound ion channel and a receptor of the neurotransmitter glutamate [4]. Along with the α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPA receptor), another glutamate receptor, it is among the most prominent excitatory synaptic receptors in the vertebrate nervous system [7]. Two unique characteristics allow the NMDA receptor to serve as a “molecular coincidence detector” [6]. One of these characteristics is that it is doubly gated [4]. Like normal neurotransmitter-gated ion channels, it requires binding of its neurotransmitter (glutamate in this case) for its channel to open [7]. However, once glutamate binding opens a NMDA receptor’s channel, a magnesium ion is attracted to the channel’s pore, which prevents ions from flowing freely through the channel [4, 7]. This magnesium ion will only become dislodged when the membrane is depolarized [4, 7]. The result of this double-gatedness is that the ion channel will only be open under the concurrence of two events: The presynaptic neuron must have fired an action potential, releasing glutamate into the synapse, and the postsynaptic neuron must be sufficiently depolarized by the collective action potentials of the rest of its presynaptic neurons. The second important characteristic of the NMDA receptor is that its channel allows calcium ions to flow into the cell [4]. The conjunction of these two important characteristics means that whenever the presynaptic neuron and the postsynaptic neuron are both firing action potentials, calcium ions will flow through the NMDA receptor into the cell (**Figure 1**). This has very important implications for the plasticity of the synapse.

The entry of calcium ions into the cell activates calcium-calmodulin-dependent protein kinase II (CaMKII) and protein kinase C (PKC) [5]. The activation of these two kinases leads to increased efficacy of synaptic transmission for that particular synapse. The mechanism by which this happens is not yet certain [5]. Two models exist, and they are by no means mutually exclusive [5]. In the first model, either CaMKII or PKC phosphorylates AMPA receptors in the synapse, increasing the amount of sodium ions that can flow through the AMPA receptors [6]. In the second model, there are vesicles loaded with AMPA receptors near the synapse, and activated CaMKII causes these vesicles to fuse with the postsynaptic membrane, increasing the concentration of AMPA receptors at the synapse [5]. Whether either or both of these models is correct, the kinases effect a change at the synapse that increases the synapse’s sodium conductance when the AMPA receptor channels are opened by glutamate released by the presynaptic cell. The increased sodium conductance means that the postsynaptic cell would become more strongly depolarized by that particular

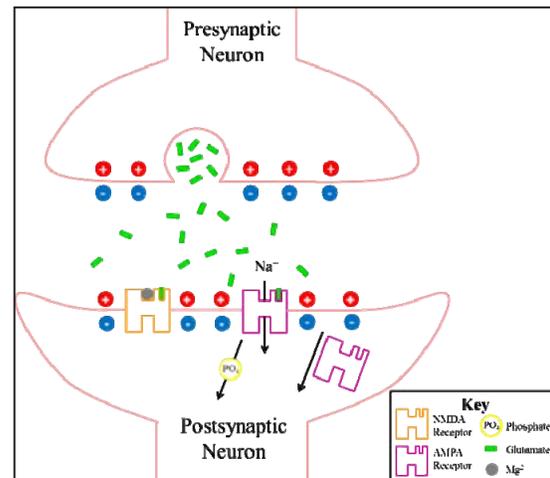


Figure 2. In the process of long-term depression, the NMDA receptors bind to glutamate released by the presynaptic neuron’s action potential, but the postsynaptic neuron is not sufficiently depolarized by its other synapses. The negative membrane potential causes magnesium ions to block the NMDA receptors’ channels, inhibiting the influx of calcium. The low calcium concentration at the synapse causes AMPA receptors to be removed from the synapse and/or causes AMPA receptors to lose sodium conductance through dephosphorylation.

synapse than it would have become if there had been fewer or less effective AMPA receptors in its membrane. Stronger depolarization means that the postsynaptic cell is more likely to fire an action potential. Thus, through the effect of the NMDA receptors' calcium intake on the activity of the postsynaptic kinases, the presynaptic cell has gained greater influence over the postsynaptic cell. This all happened because both cells were concurrently firing action potentials, just as Hebb had hypothesized [1].

Interestingly, like long-term potentiation, long-term depression also uses calcium ions as a signal to modify the synapse but in an opposite way that makes the firing of the synapse less influential over the postsynaptic cell [5]. As long-term potentiation is controlled by the NMDA receptors' regulation of calcium flow, so too is long-term depression [5]. When the presynaptic cell fires an action potential but the postsynaptic cell is not depolarized, glutamate will bind to the NMDA receptors, but they will mostly be blocked by magnesium ions. Therefore, only a small amount of calcium will seep into the postsynaptic cell. However, this small calcium concentration affects different enzymes than those activated by a large calcium concentration (**Figure 2**) [5]. Whereas high calcium concentrations activate the protein kinases mentioned earlier, low calcium concentrations activate protein phosphatases [5]. Because protein kinases add phosphate groups to proteins while phosphatases remove phosphate groups from proteins, the phosphatases do the exact opposite of what the kinases would have done. In the case of AMPA receptors already in the membrane whose sodium conductance would be increased by the kinases, the phosphatases dephosphorylate the receptors, inhibiting their conductance of sodium [5]. In the case of AMPA receptors being added to the postsynaptic membrane through a mechanism of the kinases, phosphatases serve to have AMPA receptors removed from the membrane [5].

Consolidation of Memories

The increase in synaptic strength due to the NMDA receptors' immediate effects on AMPA receptors is part of consolidation, the transformation of a memory trace into more stable long-term memory. NMDA receptors (and possibly AMPA receptors) regulate proteins such as mitogen activated protein kinase (MAPK) and the transcription factor cAMP-Ca²⁺ response element binding protein (CREB) [7]. The activation of these proteins leads to changes in gene expression that induce further LTP through changes in synaptic morphology [7]. These changes may include an increase in the density, length, diame-

ter, and overall size of dendritic spines, and doubling of synapses through a mechanism in which the synapses split in half [8, 9, 7, 4]. All of these changes involve an increase in synaptic surface area, which strengthens the presynaptic cell's influence over the postsynaptic cell. Consolidation of memories is thought to primarily take place in the hippocampus as lesions in the hippocampus eliminate the ability to form new memories but do not impair other areas of cognitive function [6]. For example, older memories are not lost in the presence of such lesions [6]. This is because consolidated memories are thought to eventually be transferred to the neocortex [10]. It seems likely that the potential for synaptic plasticity is weaker in the neocortex, making it a slower learner than the hippocampus but also more stable for long-term storage [9].

Evidence for a Link Between Synaptic Plasticity and Memory

There are two main reasons to believe that synaptic plasticity plays a major role in memory. The first reason is that synaptic plasticity grants synapses all the characteristics one would expect in a system that acquires information (learning) and stores that information (memory), including specificity, reversibility, cooperativity, and associativity [6]. Because the effects triggered by the NMDA receptors' flow of calcium are localized to a single synapse, the successful or unsuccessful firing at one synapse will not significantly affect the synaptic strength of other synapses on the postsynaptic cell. This specificity would be important in learning because without it the information content of a circuit would be lost as synapses would not be properly strengthened for their synchrony or weakened for their lack thereof. No presynaptic neurons would be any more influential than the others over the postsynaptic neuron, and memory traces would become random and meaningless. Reversibility would also be important in memory to account for updating information and forgetting information. The cooperativity required of the firing of the presynaptic neurons to depolarize the postsynaptic neuron ensures that a neuron will not take part in a memory trace unless a sufficient number of triggers elicit that memory trace. The associativity that plasticity brings to the neurons in a cell assembly means that if a significant part of a memory is brought to mind, the trace will activate the rest of the memory [11]. For example, recalling a simple mnemonic device may remind a person of other information previously associated with the mnemonic device, such as the colors in a rainbow or the order of the planets by average dis-

tance from the sun. Additionally, because of the multiplicity of pathways in a cell assembly, some synapses could disappear or weaken without destroying the entire memory. These weakened synapses would be strengthened once again by LTP if the rest of the neurons comprising the memory were activated [9]. This could partly explain why reviewing information (e.g. a student studying for a final exam) makes the information more likely to be successfully remembered in the future.

The second reason to believe that synaptic plasticity is important to learning/memory is that experimental evidence supports this theory. For instance, the blocking of the NMDA receptors inhibits hippocampal LTP and impairs learning [12]. The deletion of the gene for CaMKII, one of the kinases that increases the strength and/or number of AMPA receptors at a synapse, impaired LTP along with spatial learning [13,14]. Deletion of the gene that codes for the NMDA receptor causes severe deficiencies in LTP, LTD, and learning [15]. On the other hand, animals engineered to produce an abnormally high number of NMDA receptors exhibited augmented learning in some tasks [5].

Future Areas of Exploration

Although much has been learned about synaptic plasticity and memory in the last couple of decades, there is still much to be discovered. Not all the details of the mechanisms of consolidation are known. Recently, reconsolidation, a phenomenon similar to consolidation, has been explored [16]. The current majority view is that retrieval of consolidated memories brings about a brief wave of plasticity that allows the memory to be modified [9,16]. This updating may allow new information to be linked to or incorporated into the old memory for the purpose of synthesizing information [9]. However, this could also lead to the corruption of the memory, accounting for the potentially unreliable nature that psychologists attribute to long-term memory [16]. Another interesting phenomenon to explore is synaptic scaling [6]. The idea of synaptic scaling is that decreased neuronal activity elicits a compensatory increase in the strength of all excitatory synapses, and increased neuronal activity does the opposite [7]. The changes occur in a multiplicative way that preserves the relative strengths of synapses as well as the ratio of NMDA receptors to AMPA receptors [7]. This may happen to maintain the information content of synaptic transmission and/or to maintain a NMDA:AMPA ratio that will be conducive to adaptive gene expression [7].

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Medical Prognosis and Management of Children with Eosinophilic Disorders

Jordan D. Busing

Eosinophilic disorders are a set of diseases that are profiled by an increase in the prevalence of a type of white blood cell known as an eosinophil. These cells are normally responsible for combating parasites and controlling the mechanisms that regulate asthma and allergies. In relation to eosinophilic disorders, the dramatic increase in eosinophils signals a response to foreign substances in the body. For this reason, an eosinophilic disorder is classified as an autoimmune and inflammatory disease that is characterized by high levels of eosinophils that directly lead to inflammation in the body. Once the foreign substance has left the body, the excess eosinophils are left behind to attack the digestive tract and/or the esophagus. Eosinophilic disorders are not only becoming more common in the general population, but are specifically prevalent in highly developed countries. Typically, patients with an eosinophilic disorder exhibit symptoms such as failure to thrive/malnutrition, diarrhea, vomiting, and abdominal pain. In the majority of cases, these symptoms are triggered by reaction to food. At this time, eosinophilic disorders are still difficult to diagnose and there is no precedent on how to treat them. Parents of children with eosinophilic disorders often encounter an elongated time from symptom onset to diagnosis, varying treatment plans, and lack of research and literature on the set of diseases; however, with increased awareness and new research there is hope that management of eosinophilic disorders will be improved in the coming years.

Introduction

For the purpose of this paper, a survey of forty-six parents from a support group of children with eosinophilic disorders was conducted to determine generic data, diagnosis, and treatment plans of their respective children. Interestingly, the group of disorders appears to be more predominant in males than in their female counterparts.

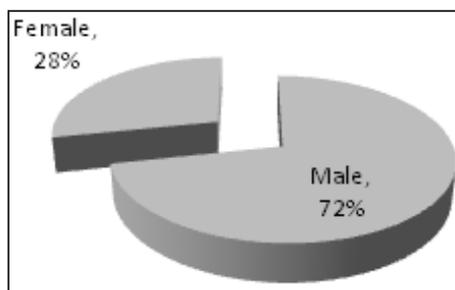


Figure 1: Classification of sex of children surveyed with an eosinophilic disorder.

Three major factors comprise a manifestation of an eosinophilic disorder: genetic predisposition, allergic genetic background and environmental exposure [1]. The overwhelming number of males with the disease confirms the aforementioned genetic predisposition to the set of diseases. Research suggests that part of the gene alteration that confirms the disease is located on the X chromosome. In males, research

shows, the Y chromosome cannot correct this gene alteration [1]. The collected here closely matches the observed dominance in male patients of other studies that were found to be 70% [1] and 75% of the diagnosed [9].

Familial Patterns

While eosinophilic disorders show some familial pattern, these patterns are certainly not present in the majority of cases. This research found that 13% of all parents surveyed had more than one child with an eosinophilic disorder. There is not observed connection between parent and child who both inherit the diseases. If the disease is observed in multiple family members, it is predominantly found in siblings [10].

Age

Because the data collected for this research were focused on children with an eosinophilic disorder, only age ranges of children 18 or younger were considered; however, it should be noted that the set of diseases is primarily found in children and is a rarity in persons over the age of 18 (Figure 2).

As shown in Figure 2, the majority of children fall within the 5-10 year age group which is slightly lower

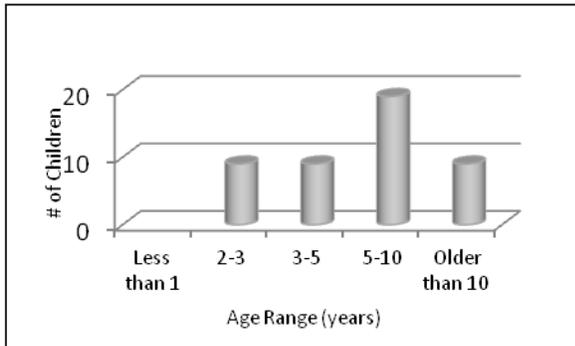


Figure 2: Age range of children identified by the study.

than the previously researched median age of 10.8 years [9]. This decrease in age dominance could likely be attributed to greater prevalence and recognition of the diseases, leading to a decrease in age at time of diagnosis.

Variety of Eosinophilic Disorders

Within the scope of eosinophilic disorders are 4 main subcategories with each affecting a different area of the digestive and esophageal tract. Among these are Eosinophilic Esophagitis (EoE), Eosinophilic Gastritis (EG), Eosinophilic Gastroenteritis (EGE), Eosinophilic Colitis (EC) [6]. The suffix of each diagnosis describes the area affected. EoE is characterized by elevated eosinophil levels in the esophagus. EG is characterized by elevated eosinophil levels in the stomach, while EGE is a combination of the stomach and small intestine. Likewise, EC is characterized by high number of eosinophils in the large intestine [6].

Elevated eosinophil counts are not always an indicator of an eosinophilic disease and can be elevated as a result of other autoimmune and inflammatory diseases [3] and an individual may be diagnosed with multiple classifications of eosinophilic disorders. Among these classifications of diseases, EoE comprises the vast majority of eosinophilic disorders compared with other three diagnoses. As shown in Figure 3, EoE outnumbers other eosinophilic disorders greatly, and therefore the majority of research focuses on EoE. These data also match past research studies that have found ~90% of children with an eosinophilic disorder exhibit some form of EoE [1].

Current Treatment of Eosinophilic Disorders

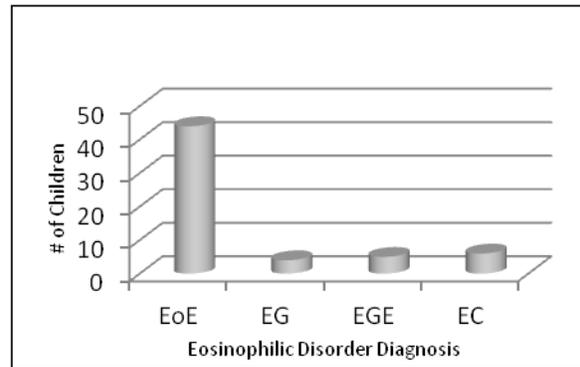


Figure 3: Frequency of each subgroup of eosinophilic disorders in the study.

As mentioned in the abstract, eosinophilic disorders are still relatively new on the medical scene and many treatments are still on a trial and error basis and often patients undergo a combination of treatments. Figure 4, below, shows the current treatment plans for the patients studied.

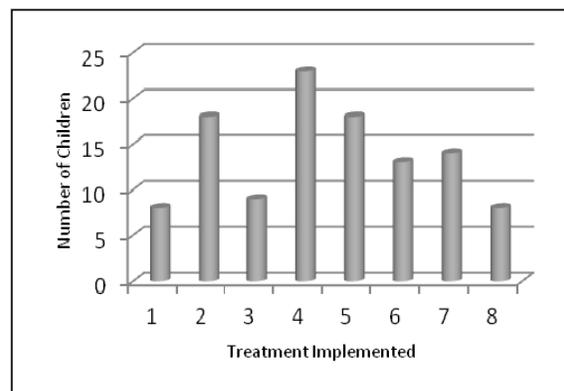


Figure 4: Treatment of patients identified, with number on x-axis corresponding to the following:

1. Amino acid based formula diet – crystalline amino acid based elemental diet, currently considered the best treatment with ~90% remission of symptoms [3, 4, 10].
2. Targeted elimination diet – Patients try to identify food triggers in their diet and try and eliminate them in stepwise fashion. Close to 75% success rate [10].
3. Empiric 6 food elimination diet – diet that restricts cow-milk protein, seafood, peanut, egg, wheat, and soy, in any form. Also has a relatively good success rate with improvement of symptoms in 74% of patients in

one study [4].

4. Food trials – Implemented while on amino acid based elemental diet, patient reintroduces individual food into diet one at a time.
5. Acid suppressor – such as Nexium, often used in combination with one of the above diets.
6. Oral viscous budesonide – designed to coat the esophagus in EoE patients to relieve inflammation [7].
7. Feeding tube – used for treatment of eosinophilic disorders when formula uptake is inadequate or child exhibits absorption problems. Can either be an nasogastric intubation, which is run through the nose into the stomach or enteral feeding tube where it is placed directly into the digestive tract.
8. Swallowed systemic steroids – used only when above dietary treatments are deemed unsuccessful [3].

There are several difficulties with the aforementioned treatment plans. First, many of the restrictive diets are dependent upon strict patient adherence, but because the patients are often children, adherence is poor [8]. It is nearly impossible for parents to monitor their child every minute of the day. Also, the elemental formula has a foul taste and is difficult to drink daily, hence the implementation of feeding tubes in some patients. Second, the short term and long term psychological impact on patients has not been determined. Klinnert stresses that not only do the children experience stress and anxiety, but the parents do as well [5]. Already anxious because their child is chronically ill, parents' stress is furthered by the lack of research, literature, and concrete treatment for eosinophilic disorders. Franciosi et. al. go even further to define parental and child concerns with the disorders outlining a few problems such as feelings of being different, difficulty coping with symptoms, anxiety in food related situations, and, as described above, diet and medication adherence [2]. Overall, more studies are needed to fully understand the scope of treatments and psychological effects on patients dealing with eosinophilic syndromes.

Diagnosis Time

Recognition, treatment, and knowledge about eosinophilic disorders are growing, but understanding

of the disease is still only in its infancy. Because it is so new, physicians often misdiagnose the disease as another inflammatory disease or refer the patient to another physician. Parents of children with eosinophilic disorders often find that a correct diagnosis of their child not only takes time, but in fact, it can take up to several years in the majority of cases.

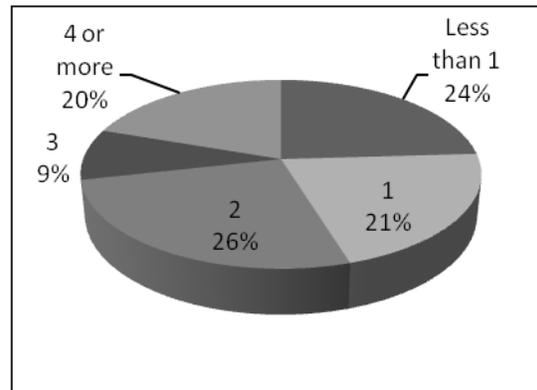


Figure 5: Diagnosis time (in years) of children studied.

As seen in Figure 5 above, the majority of cases take 2 years to diagnose, while a staggering 20% of cases take 4 or more years to obtain an accurate diagnosis. While diagnosis time is improving, more widespread, knowledge is needed among the scientific and medical community to decrease time from symptom onset to diagnosis time.

Physician Distance

Another problem that stems from the recent arrival of eosinophilic disorders diagnoses nationwide is the proximity of patients to their physicians.

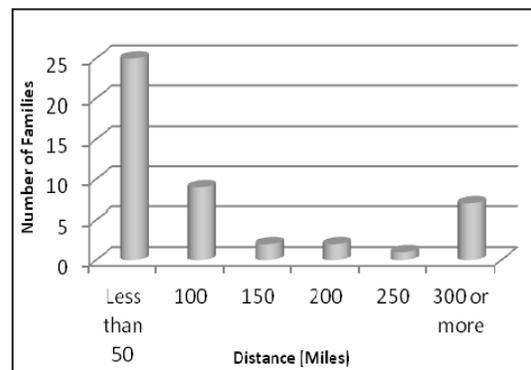


Figure 6: Proximity of families to the physician that treats the eosinophilic disorder.

As shown in Figure 6, many families live less than 50 miles from their primary caregiver, but alarmingly, 7 families were over 300 miles to their physician and nearly 50% had to travel 100 miles or more. Medication and the elemental formula are expensive; this proximity problem only adds to the stress of a family and patient managing an eosinophilic disorder.

Satisfaction of Care

With the lack of knowledge, difficult diets, and anxiety of a chronic illness, parents were asked if they were currently satisfied with the current care of their child. Forty-one percent of parents claimed they were not satisfied with current treatment; however, with a lack of options, most are forced to stick to their current regimen even though they are unhappy with the results.

Conclusion

Current treatments seem to be a temporary solution to a permanent problem, often subjecting the family and patient to psychological anxiety, stress, and social wellbeing to maintain physical health. As awareness and research about eosinophilic disorders increase, hopefully so will the treatment options and physician knowledge.

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Environmental Risk Factors, Prevention, and Cost of Vascular Dementia

Mallory Des Champs

This paper explores published articles that focus on environmental risk factors, prevention, and cost of vascular dementia (VaD). Grand, Caspar, & Macdonald (2011) define vascular dementia as "a clinical syndrome of acquired cognitive and functional impairments resulting from the effects of cerebrovascular disease". The literature on VaD suggests that a healthy heart leads to a healthy brain [12,]. Research suggests that increasing physical activity, improving diet, engaging in healthy social habits and abstaining from substance abuse reduce cardiovascular risk factors, therefore reducing the risk of VaD [1, 14, 21, 24, 25, 29-32]. Also, VaD is currently the most expensive type of dementia [20]. Current and projected costs of dementia are explored within this review [4, 7, 20, 21, 27, 39, 42]. This paper focuses on methods for promoting a healthier society and lowering healthcare costs through the prevention of VaD.

Introduction

Vascular dementia is the second most common type of dementia [15]. By understanding environmental risk factors, the prevalence of this common type of dementia could be reduced. Ongoing research suggests that the health of the heart is closely linked to the health of the brain [12, 25]. The objective of the current literature review on vascular dementia is to discuss the environmental risk factors for VaD and the role of the individual in reducing this costly disease.

Environmental Cardiovascular Risk Factors

Research has identified many preventable cardiovascular risk factors for VaD [24, 14, 39]. Stephan and Brayne (2008) composed a review article on the risk factors for VaD to determine if a cost effective and safe solution exists to reduce the prevalence of dementia in the population. Low levels of physical activity and poor eating habits are associated with cognitive decline [39]. Their review also shows evidence for diabetes mellitus, hypertension, congestive heart failure, dietary fat intake, high cholesterol, obesity, and history of stroke as established risk factors for VaD [8, 31]. This finding suggests that increasing physical activity and establishing healthy eating habits lowers the risk for VaD; however, Stephan and Brayne (2008) acknowledge that no evidence has yet been found to suggest that pharmacological or non-pharmacological interventions in VaD can prevent dementia. The review also examines VaD and substance abuse, finding that excessive alcohol consumption and smoking is linked with cognitive decline [3C, 31]. Furthermore, Stephan and Brayne suggest that the aggregation of risk factors increases the likelihood of developing dementia as op-

posed to the risk associated with each factor independently. There appears to be no preemptive action that can significantly prevent dementia across the population.

Similarly, Fillit et al. (2008) conducted a literature review on the relationship between cardiovascular disease risk factors and dementia. The number of individuals living with dementia is expected to reach 81.1 million by 2040 [13]. Poor management of lifestyle risk factors such as obesity, lack of exercise, smoking, and drinking may increase cognitive decline in later life [44]. Obesity and hypertension increase the risk for cognitive decline, and increased physical exercise decreases the risk for dementia [26, 44]. Diabetes mellitus generally results from poor diet and low levels of physical activity [14]. Diabetes mellitus, a cardiovascular risk factor, increases risk for dementia [16]. Literature results are contradictory regarding the link between smoking and cognitive decline, but suggest that moderate alcohol intake may protect against cognitive decline whereas excessive alcohol intake may increase the risk for dementia, stroke, VaD, and Alzheimer's disease [10]. This review of literature also discusses the psychosocial factors such as living alone, lack of close social relationships, and limited social interactions [14]. Higher amounts of social activity correlate with decreased risk for dementia [15]. With the estimated increased prevalence of dementia, it is important for physicians to pursue interventions for cardiovascular risk factors to reduce the incidence of dementia.

Kalaria et al. (2008) reviewed the literature on the risk factors for dementia in developing countries. Particularly for VaD, the necessary routine neuroimaging in the diagnosis process is not readily available in

developing countries, thus complicating diagnosis of the disease. Records show that the prevalence of VaD is relatively low in developing countries compared to developed countries [33]. Specifically, VaD is more common in Southeast Asia and China compared to Eurasia and India [3]. Tobacco, which is common in China, decreases vascular function influencing cognition [2]. Overall, these authors concluded that diagnosing VaD is difficult in developing countries due to the lack of medical access; however, their reviewed literature identified hypertension, diabetes mellitus, obesity, and tobacco as risk factors of dementia [9]. VaD is an issue that needs to be addressed in both developed and developing countries.

Furthermore, Grand et al. (2011) reviewed the current state of knowledge for dementia research including VaD. Longitudinal studies conclude a significant association exists between hypertension and VaD [5]. The authors highlight the importance of reducing cardiovascular risk for a healthier brain, thus lowering the risk for cognitive impairment later in life. Early disease identification and successful intervention is necessary in reducing cognitive decline and preventing dementia [7]. The earlier the disease can be identified, the greater the potential for slowing progression. While it is clear that dementia is an expensive disease, it is estimated that the financial burden of dementia will double each decade [7]. Future research seeks to promote preventative lifestyle behavior programs and a healthcare system capable of supporting the growing number of individuals afflicted with dementia.

Knopman and Roberts (2010) conducted a meta-analysis similar to Stephan and Brayne's review article to determine VaD risk factors [24]. Their findings suggest that obesity is a predictor for VaD which affects the brain. Knopman and Roberts (2010) conclude that midlife obesity directly or indirectly adversely affects the brain [24]. This review also observed that risks for dementia are higher if diabetes mellitus is diagnosed early rather than later [24]. Conclusively, diabetes mellitus is associated with later life cognitive decline [23]. Finally, hypertension is a fairly prevalent issue affecting a majority of middle to late aged adults. Hypertension may lead to brain injury [41]. This finding suggests that brain injury may increase the risk of vascular dementia [41]. If hypertension, a prevalent medical issue can be reduced, the prevalence of VaD is likely to be reduced. While Stephan and Brayne (2008) previously concluded there are currently no successful intervention methods for preventing dementia, Knopman and Roberts (2010) suggest that there may be some preventive measures that can be taken during midlife before cognitive decline

begins.

Monsuez et al. (2011) composed a literature review of midlife cardiovascular risk factors and dementia. Medical records suggest that diabetics who previously suffered a stroke were at an increased risk for VaD [28]. Both diabetes and stroke are risk factors for VaD [28]. Also, these authors found large-scale epidemiologic cohort studies correlating midlife hypertension with cognitive decline [40]. Anti-hypertensive treatment reduced the incidence of dementia, cognitive decline, and the combination of cognitive decline and recurrent stroke [38]. Another cohort study associates an increased risk of dementia with lower levels of physical activity during midlife [30].

Prevention

While medical science has not advanced enough to cure dementia, the next best option is prevention. Monsuez et al. (2011) examined prevention of VaD in later life by increasing physical exercise and adopting a Mediterranean-type diet. Two cohort studies concluded that a Mediterranean-type diet and increased physical activity are associated with a lower risk of dementia [11, 37]. Consistent with the literature review by Stephan and Brayne (2008), Monsuez et al. (2011) concluded that cardiovascular risk factors for VaD have been identified, but no significant difference is observed in cognitive decline and the intervention techniques. Similarly, Kalaria et al. (2008) reviewed the literature on prevention of dementia specifically using traditional diets and medicinal plants in prevention. Lifestyle and diet changes are the most cost effective solution to prevent dementia [9]. Low calories, low fat, high vegetable, and some fish intake may be protective against cognitive decline [19]. However, tofu is correlated with worsening memory [43]. Additionally, research may gain an invaluable resource for new anti-dementia therapies through traditional herbal medical practices conserved in developing countries [32]. This review offers possible alternative methods for research in preventing dementia.

Aarsland et al. (2010) conducted a systematic review of 24 longitudinal studies to examine physical activity as a preventive measure for VaD. The meta-analysis included reviews of studies measuring the effect of low and high physical activity across people with and without VaD. Twelve of the reviewed studies examining the effects of physical exercise of VaD showed evidence for increased physical exercise as a predictor for a decreased risk of developing VaD [1].

While Aarsland et al. (2010) support increased physical activity as a preventative measure for VaD, they acknowledge that there were few participants in the reviewed studies and other confounding variables such as smoking, diabetes, diet, cholesterol levels, and cardiovascular disease that may have influenced the studies' findings. Larger scale experiments are necessary to more accurately evaluate the role of physical activity in VaD prevention.

Furthermore, Middleton and Yaffe (2009) conducted a literature review examining promising strategies for preventing dementia. Middleton and Yaffe (2009) estimate that by 2050, the prevalence of dementia will have tripled. Evidence suggests that physically active people generally decline cognitively slower than less physically active people [35, 36]. Similar to Fillit et al. (2008), higher levels of social engagement might reduce the risk of dementia by maintaining their cognitive performance through increasing cognitive reserve. This finding suggests that maximizing cognitive reserve may delay the onset of dementia. This literature review proposes that increasing cognitive and physical activity, engaging in social interactions, and implementing a healthy diet could reduce the prevalence of dementia [29].

Poor eating and exercise habits correlate with society's increased cardiovascular problems, which may have contributed to the increased prevalence of dementia, specifically VaD. In societies with fast food, public transportation, and sedentary lifestyles, addressing cardiovascular risk factors for VaD is vital.

Cost

Current research on the healthcare costs of dementia informs people about the potential economic costs of this disease. Current research seeks to compare individual versus societal costs and explore future costs of VaD.

Banerjee and Wittenberg (2009) examined the costs and benefits of early diagnosis and intervention for dementia and estimated the savings based on England's population for both individuals and the overall public by delaying admissions to care homes [4]. They developed a model to determine their estimations. Incorporating the early diagnosis and interventions, the estimated costs are around \$340 million annually [4]. It is proposed that delaying admissions to care homes would significantly reduce costs for public funds. For example, the projected costs at 10% admissions reductions for public funds for Year 4 and Year 10 were about \$70 million and \$185 million respectively [4]. The authors also believe there would be significant individual and family savings. For exam-

ple, the projected costs at 10% admissions reductions for individual and family funds for Year 4 and Year 10 were about \$70 million and \$196 million respectively [4]. Overall, reduced admissions could substantially save money for the individual, family, and public.

Luengo-Fernández et al. (2006) also reviewed costs in England; however, they examined healthcare and non-healthcare costs of cardiovascular disease [27]. Increasing costs for cardiovascular disease correlates with increasing costs for dementia [27]. These authors used epidemiological and resource use data to evaluate the burden of cardiovascular disease. For the healthcare expenditure, community health and social services, primary care, hospital outpatient care, accident and emergency cost, hospital inpatient care, hospital day cases, cardiac rehabilitation, and drugs were all examined in determining this estimate. For England, it was determined that 12.1%, 0.9%, and 6.6% were due to cardiovascular disease, coronary heart disease, and cerebrovascular diseases, respectively [9]. Non-healthcare expenditure included informal care and productivity losses. For informal care, the information is not directly available, but can be estimated. Based on surveys, most people over age 65 reported receiving at least some informal care due to cardiovascular issues [6]. Cardiovascular disease healthcare costs represented the most expensive component of cardiovascular disease at 63% [22]. Results show that healthcare costs of cardiovascular disease account for greater costs than non-healthcare costs. Considering these results, the prevalence and cost of VaD will continue to be an issue unless cardiovascular diseases can be resolved.

Hill et al. (2005) compares the healthcare use and costs of dementia in a community-dwelling population [20]. The authors examined VaD, Alzheimer's disease, other dementias, cerebrovascular disease without dementia, and patients without dementia or cerebrovascular disease. Using medical claims and records, the authors estimated that VaD had the highest annual costs at \$14,387. Also, admissions for VaD were higher compared to the other types of dementia. Specifically VaD patients had significantly higher amounts of hospital admissions and hospital days compared to individuals without dementia or with other types of dementia. VaD is the most expensive type of dementia due to the extra cost of caring for the cerebrovascular conditions that do not afflict patients with Alzheimer's disease [20].

A more recent article examines the cost of dementia in 2009. The estimated cost of dementia rose from \$315 billion worldwide in 2005 to \$422 world-

wide in 2009 [42]. Seventy-five percent of this cost occurred in the developed countries in North America and Europe. The United States has by far the highest costs for dementia. Their approximate cost of dementia in 2009 is “based on the estimated prevalence of dementia in different countries and regions of the world, cost of illness studies from different countries, and studies of the amount of informal care” [42]. The average worldwide annual cost is estimated at \$12,200 per individual with dementia. In the United States, the annual cost is \$26,700. As of 2009, the number of individuals with dementia rose to right over 34 million. It is probable that as of 2011, this number has continued to rise. If ADLs and IADLs were considered in the total cost, then the worldwide annual cost would be \$608 billion as opposed to \$422 billion which only include ADLs. The authors’ main goal of this estimation is to emphasize the enormous impact of dementia on the economy. Proper organizing and finance care for individuals with dementia is a difficult challenge facing the healthcare system [42].

Comas-Herrera and colleagues took another approach to exploring the costs of dementia [7]. Comas-Herrera et al. (2011) used the Delphi technique to gather experts’ opinions on the projected costs of dementia by gathering experts’ opinions on its projected costs in the next 50 years [7]. Though only 19 experts comprised the panel, a low number of participants that limits the usefulness of this study, most of the panel expects a small reduction in the prevalence of dementia, a freeze in the number of older people in nursing homes, and an increase in the qualifications and pay of caregivers in nursing homes. This optimistic prediction stems from the panel’s belief of future improvement in dementia prevention.

Discussion

The purpose of this literature review was to explore the environmental risk factors for VaD and discuss prevention of this disease. This review of the literature explored the connection between cognitive decline, specifically vascular dementia, and risk factors such as obesity, diabetes mellitus, hypertension, alcohol abuse, and excessive smoking. Also this review discussed possible ways to decrease the prevalence of vascular dementia through increased physical activity and healthy eating habits. Furthermore, this review examined current and predicted costs of VaD. Informing the public about the preventable risk factors for dementia could lead to a decrease in the prevalence of VaD thus decreasing the spending on this disease.

Research suggests that reducing cardiovascular issues will decrease risk for cognitive decline [4, 18, 25]. One crucial component of reducing the incidence of VaD is promoting heart health. Several implicated cardiovascular risk factors, obesity, diabetes mellitus, hypertension, substance abuse, and poor social interactions are all considered risk factors for developing VaD [1, 14, 18, 21, 24, 29, 30, 39]. All of these risk factors above are preventable if a patient is willing and able to be proactive about their daily health.

The main issue the articles did not agree on was whether VaD could be prevented. One side of the research argues that VaD cannot be significantly reduced [30, 39]. The other side of the argument states that VaD can be significantly reduced if individuals reduce the incidence of risk factors for VaD [18, 10]. Further research into preventative interventions for VaD will be required determine if this is a preventable disease. Prevention of this disease is essential in estimating projected healthcare costs.

There are several limitations to this literature review. Some of the review articles included few participants [1, 7]. The Delphi panel only had 19 expert opinions [7]. Also the previous and current costs of dementia are estimates; however, the estimates are based on current information and trends. [4, 20, 21, 27, 42]. Suggestions for future research include more research exploring the relationship between substance abuse and VaD and a larger panel similar to the study by Comas-Herrera et al. (2011) to research the projected costs of VaD.

In general, dementia is a costly burden for both the individual and society. The estimated cost for dementia treatment was \$422 billion worldwide in 2009 [42]. As the population increases, the number of individuals with dementia will also increase. Also, obesity has become a major issue for developed countries. With obesity comes a majority of the risk factors for VaD. Due to these predictions, it is vital to address the healthcare cost issue of dementia. Possible traditional medicinal plants in developing countries are another outlet to explore for prevention and intervention [21]. Banerjee and Wittenberg (2009) researched decreasing costs of dementia over time in England through delaying admissions to care homes. Luengo-Fernández et al. (2006) determined that healthcare costs of cardiovascular disease account for greater costs than non-healthcare costs. Cardiovascular disease, a risk factor for VaD, has a high healthcare expenditure. With a high expenditure for cardiovascular disease, high costs for VaD can be expected. Preventing and lowering the prevalence of cardiovascular disease will ultimately lower prevalence for VaD.

With increased life expectancy, the prevalence of dementia will continue to increase unless a pharmacological or non-pharmacological treatment is discovered. VaD presents both a detrimental and costly issue to the individual, relationships, and society. Fortunately, emerging research suggests that VaD can be reduced through increased exercise, positive social experiences, and a healthy diet. Further research on the relationship between cardiovascular risk factors and VaD can aid future diagnosing and treatment of VaD. The results of this literature review stress the importance of understanding the preventable risk factors for this disease, allowing researchers to devise successful prevention plans. Successful prevention plans should lead to a decreased prevalence of individuals living with dementia, thus decreasing worldwide economic burden of dementia.

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