Hendrick Hudson
High School

Science Research

May 2015

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" You are limited only by your imagination"

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Science Research

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Dr, Christine Rogers received a 2015 INTEL STS Badge and a Teacher of Merit Award.

Jazz Munitz is a semi-finalist for INTEL STS and Siemens Competitions.

Jordan Hudock received a badge for her entry to the INTEL STS competition.

This year has been another amazing year for the Science Research Program. Jazz Munitz was a INTEL Science Talent Search and Siemens Competition semi-finalist for his excellent paper on how nanoparticles can be engineered to target and kill cancer cells, hereby opening the door to widely available efficient and cost effective treatments. The INTEL STS as well as the Siemens competition are two of the most prestigious competitions and both are paper-based. Jazz also placed Third place in the Junior Science and Humanities Symposium (JSHS), allowing him to compete at the upstate JSHS in Albany with a poster, where he took First place in his category. He got Second Place at the Westchester Science and Engineering Fair (WESEF) and first place at the Tricounty Fair, becoming a New York State Congress Finalist. Jazz worked with Dr. Willem Mulder in Mount Sinai Medical Center, and will join Cornell University in the fall with plans to continue his research. His paper (which excerpt is to be found here) is to be submitted soon in American Chemical Society Bioconjugate Chemistry Journal.

Jordan Hudock won Second Place at WESEF in the Behavior category for her work on stress and meditation, under the guidance of Dr. Emily Stern at Mount Sinai Medical Center. Jordan did a remarkable work, designing and conducting all experiments by herself on Hendrick Hudson Students volunteers. Jordan has been able to share a lot of her interest and a wisdom beyond her years through this project. Undertaking such responsibilities gave her great insight in how research is done and was an invaluable experience for her.

Many Science Research Program alumni have continued their work once in college and have benefited from this outstanding experience, acquiring essential skills to be successful in college.

Microfluidics-Facilitated Synthesis and Characterisation of Apoptosis-Inducing Low-Cost Nanoparticles for Cancer Therapeutics, by Jazz Munitz, INTEL STS Paper excerpt.

Abstract

In recent years, the field of nanomedicine has become increasingly important and intriguing in the biomedical and biopharmaceutical communities. Nanomedicine, or the "development and application of nanoparticles for biomedical purposes", describes a broad range of research fields, which converge on the biomedical utilization of structures ranging from 2-100 nm in size. In this study, two apoptosis-inducing nanoparticle formulations have been developed, synthesized, characterized, and tested in vitro on cancer cell lines. The microfluidics-synthesized nanoparticle formulations displayed favorable drug encapsulation and release features, long-term stability, as well as the ability to include imaging labels. Their ability to have a high cytotoxic effect on cancer suggests possible use as platforms for treating solid cancerous masses.

Introduction

The use of nanoparticles for the treatment of ailments is becoming increasingly relevant. Beginning with the first documented commercialization of magnetic nanoparticles in the 1990's (1), the field of nanomedicine has experienced exponential growth resulting in a wide array of products and novel concepts that are both clinically and commercially relevant. While the field of nanomedicine is a relatively new area of study, some of the key concepts exploited and utilized by researchers were discovered prior to the nanoboom of the late 1990's and early 2000's.

One such discovery is the enhanced permeability and retention (EPR) effect, a peculiar and useful phenomenon for nanoparticle tumor targeting. In order for tumors to grow at rates that surpass rates of growth demonstrated by normal body cells, they must gain nutrients in larger volumes. The tumor cells stimulate the growth of new blood vessels through the vascular endothelial growth factor, or VEGF, a protein that both tumor cells and healthy cells secrete in order to stimulate the process of both vasculogenesis as well as angiogenesis. This results in the availability of fewer nutrients for healthy cells, thus contributing to the disease's many harmful effects on the body. Through the over-use of VEGF, vascular diseases and disorders can develop, further adding to the damage tumor cells can cause on the body, and resulting in morphologically strange vasculature structure such as enlarged and misshapen vessels which results in the EPR effect. This proves very useful in finding and treating tumors through the use of nanoparticles, as these particles are up taken into the micro-vortices in the blood stream caused by the enlarged tumor-leading vessels so long as the nanoparticles are between 10-100 nm in size. (4) The EPR effect gives nanoparticle developers and researchers a framework to design delivery vehicles that will reach the tumor cells, but not normal healthy cells.

One formulation concept, micellar nanoparticles, has opened up the possibility of transporting hydrophobic compounds into aqueous environments, such as the blood stream and interstitial fluid of tumor clusters. "Micelles — biocompatible nanoparticles in which poorly soluble drugs can be encapsulated — represent a possible solution to the delivery problems associated with such compounds and could be exploited to target the drugs to particular sites in the body." (8) Micelles are formed from amphiphilic molecules, such as block copolymers that were used in this study. An amphiphilic molecule has both hydrophobic and hydrophilic parts. In a micelle, as well as one of the

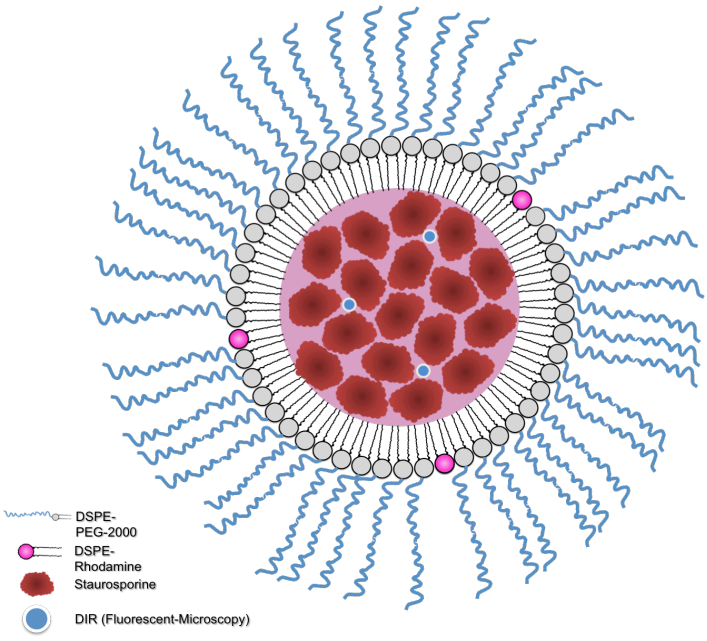

Figure 1: Schematic depicting proposed and conceptual structure of the LM platform.

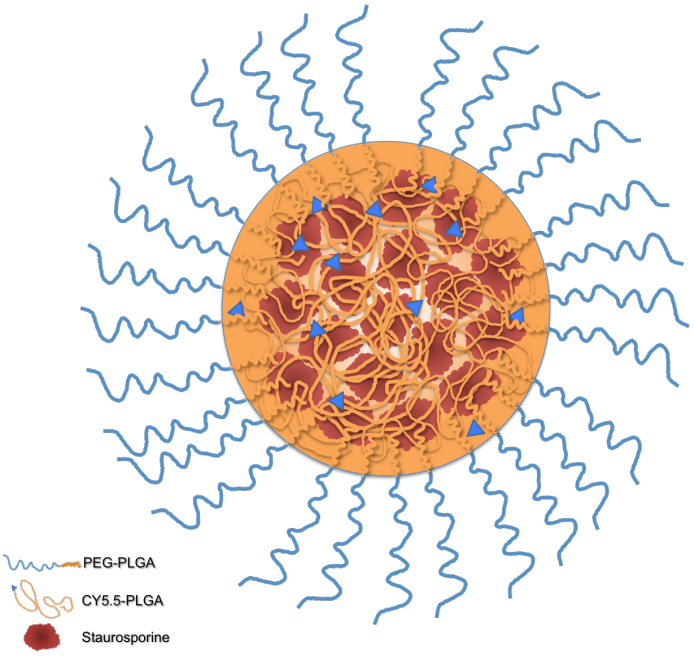

Figure 2: Schematic depicting proposed and conceptual structure of the BCP platform.

formulations developed in this study, the hydrophobic tail points itself towards the inside of the particle, as the center contains the hydrophobic drug-made core, which is nonpolar, while the hydrophilic head points itself outwards towards the water environment, which is polar. The resulting three-dimensional nanosphere acts as a barrier that entraps hydrophobic drugs, imaging dyes, or polymeric core materials. In both nanoparticle formulations developed in this study, a pegylated block was utilized to increase the hydrophilic side of the lipid/polymer, which decreases the size of the nanoparticles, while also providing a neutral shielding from the mononuclear phagocyte system and cancer cell surface recognition proteins. This pegylation technique effectively masks the nanoparticle from the body's natural defenses against foreign structures, and allows for the nanoparticle to reach tumor sites without being recognized and destroyed by the immune system.

In this study, the goal was to entrap a particularly cytotoxic compound. Staurosporine is an extremely potent compound isolated from Streptomyces Staurosporeus. This tyrosine kinase inhibitor was originally utilized in the 1980's as a model apoptosis inducer to study the process of apoptosis, or "cell-suicide". (7) Staurosporine works from two different pathways of apoptosis-induction, as it can induce cell-death either from an extrinsic pathway by activating caspase-3 and subsequently beginning the "domino-effect" caspase cascade resulting in apoptosis, or from an intrinsic pathway via multiple actions, made possible by the various binding sites of the staurosporine molecule. (13) This bi-pathway ability of staurosporine makes it an extremely good choice for a cancer-drug, specifically when encapsulated in a nanoparticle, as nanoparticles which burst within the cancer cluster will release staurosporine to act on extrinsic pathways of surrounding cancer cells, while nanoparticles which go through endocytosis or macropinocytosis by the cancer cells, will release staurosporine to work via the intrinsic pathways of apoptosis.

The synthesis of nanoparticles has traditionally been done through the process of either lipid film hydration or nanoprecipitation methods. While both techniques result in the formation of nanoparticles, these methods are time consuming and leave much room for human and production error. As this study aims to develop nanoparticle formulations for commercially usable and producible nanoparticles, consideration of time, complexity, and cost of production were extremely important factors. Therefore, in this study, the technique of microfluidics was utilized for the method of synthesis. Microfluidics is a recently developed technology that is gaining much traction in the biomedical field and scientific research community for its use in the development of "labs on chips". In the production of nanoparticles, microfluidics can be used to force the creation of micelles through a three-channel system. The microfluidics chip used in this study consists of a glass plate with a polymeric etching of a cross-formed with microvessels, which allows for the loading of synthesis materials via syringes and automated syringe-plungers. The resulting nanoparticles and solvents are pumped through the single channel after mixing in the tri-channel junction, and are expelled at the output port of the microfluidics chip. This mixing of hydrophobic and amphiphilic nanocarrier materials with the hydrophilic aqueous environment at the center tri-point, results in rapid and efficient nanoparticle formation with envisioned scalability for large-scale production, and whose output can be easily concentrated and analyzed, suggesting further ease of pharmaceutical usability. (12)

In this study, the resulting nanoparticles were analyzed for structure and composition using DLS, or Dynamic Light Scattering to analyze nanoparticle size and uniformity. (10) As well, HPLC, or High Performance Liquid Chromatography was used to quantify entrapment and concentration of staurosporine during the synthesis process. (2) Stability of nanoparticles in water, PBS, and varying percentages of buffered serum was then measured using DLS, and imaging of nanoparticles was performed by transmission electron microscopy (TEM). (11) Nanoparticle drug release profiles were then collected with the use of dialysis cassettes in PBS, and staurosporine

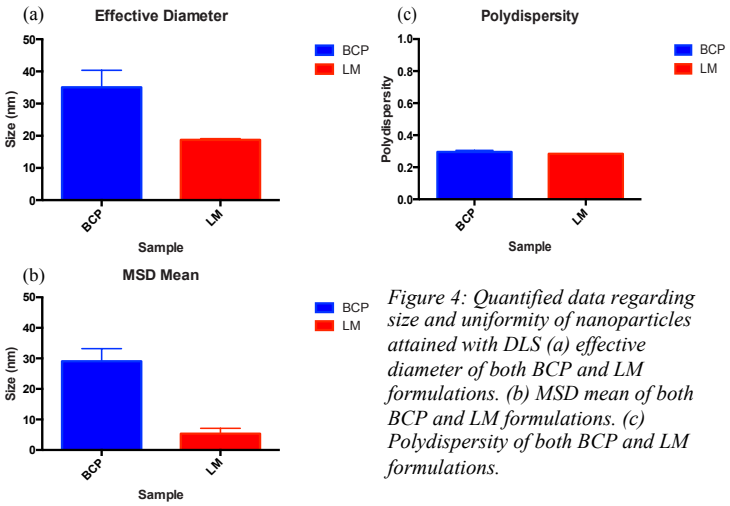

Figure 4: Quantified data regarding size and uniformity of nanoparticles attained with DLS (a) effective diameter of both BCP and LM formulations. (b) MSD mean of both BCP and LM formulations. (c) Polydispersity of both BCP and LM formulations.

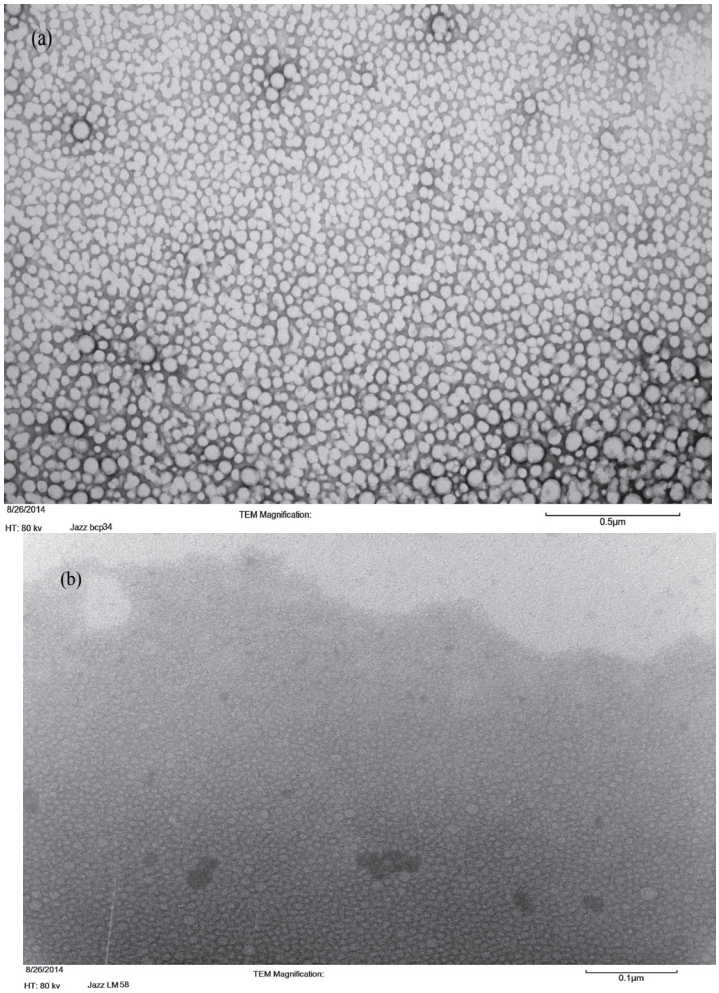

Figure 5: (a) TEM of BCP formulation by negative staining techniques. (b) TEM of LM formulation by negative staining techniques.

concentration was quantified by straightforward UV-Vis spectrophotometry methods. The in vitro cytotoxicity of nanoparticles was then determined using an MTT assay, and referenced with nanoparticles without cytotoxic agent, to observe cytotoxicity of the nano-carrier itself. Finally, fluorescent microscopy was utilized to confirm endocytosis of nanoparticles, as well as imaging capability of nanoparticles by and within cancer cells.

The goal of this study was to develop two nanoparticle-based cytotoxic-agent and imaging-dye carriers, which have different compositions but similar synthesis methods by microfluidics. Both formulations allow for the encapsulation and transportation of the specifically chosen drug, staurosporine, and imaging agents, rhodamine or cy5.5. The development of these two unique formulations allows for the quantification of their respective therapeutic and imaging capabilities, which gives insight into the relative benefits of these two nanotechnological formulation concepts. These two nanoparticle formulations were investigated as they represent two technologies from different nanomedicine approaches. Both of these formulations should meet and possibly exceed the biodynamic and biopharmaceutical capabilities of previously developed nanoparticle formulations.

(...)

Results

Synthesis of nanoparticles

Synthesis by microfluidics:

Lipid Micelle (LM) and Block Co-polymer (BCP) Formulation: For both formulations, the proposed methods and protocols for microfluidics designed for this study were followed, and the nanoparticle mixture extracted from the microfluidics process was clear, indicating no aggregation or unexpected structural failure. For the BCP formulation, the output was slightly blue, as a result of the cy5.5 dye, while the LM formulation was slightly pink, as a result of the rhodamine. The color of the output indicates that the materials introduced in the input were still present in the produced solution.

Concentration by vivaflow centrifugation:

Lipid Micelle (LM) and Block Co-polymer (BCP) Formulation: Both nanoparticle formulations were concentrated, and the lack of an either blue (BCP) or pink (LM) hue in the filtered waste indicates that the nano-carrier materials were integrated into the nanoparticles formed by microfluidics. Subsequently, the deep color of the remaining filtered solution indicates the successful concentration of the synthesized nanoparticles.

Analysis of nanoparticle size

Size analysis by DLS:

Lipid Micelle (LM) and Block Co-polymer (BCP) Formulation: Following the same protocol as described in section 2.4 of materials and methods, the size by effective diameter, size by MSD mean, and the polydispersity of nanoparticle batches were analyzed. For the BCP formulation, nanoparticles were measured to be between 30 and 40 nm in size according to both effective diameter and MSD mean analysis. For the LM formulation, nanoparticles were measured to be between 15 and 20 nm according to effective diameter, and around 10 nm according to MSD mean. While there is dispute in the field as to which analysis method, (MSD mean or Effective Diameter) is the most accurate, later in vitro analysis confirmed that the nanoparticles were within the range of size necessary for endocytosis, and according to the principles of the EPR effect, both measurements still fall within the 15-100 nm (+/- 5) range for tumor leaky vasculature exploitation, while later TEM analysis revealed imaging of nanoparticle size.

Imaging of nanoparticles

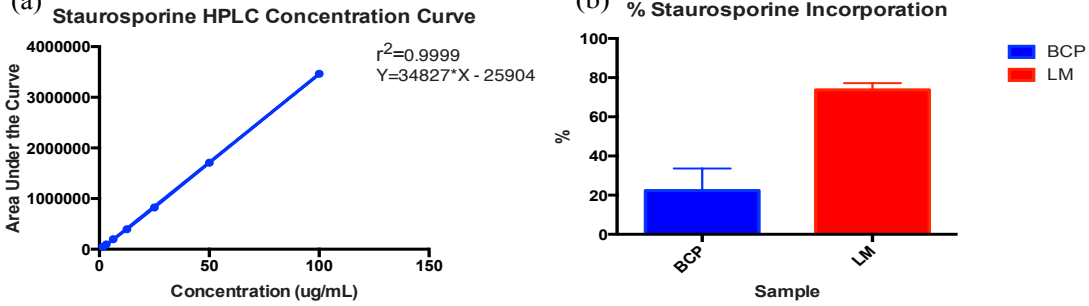

Figure 6: (a) concentration curve for staurosporine using HPLC analysis. (b) Interpolated percentage of staurosporine incorporation.

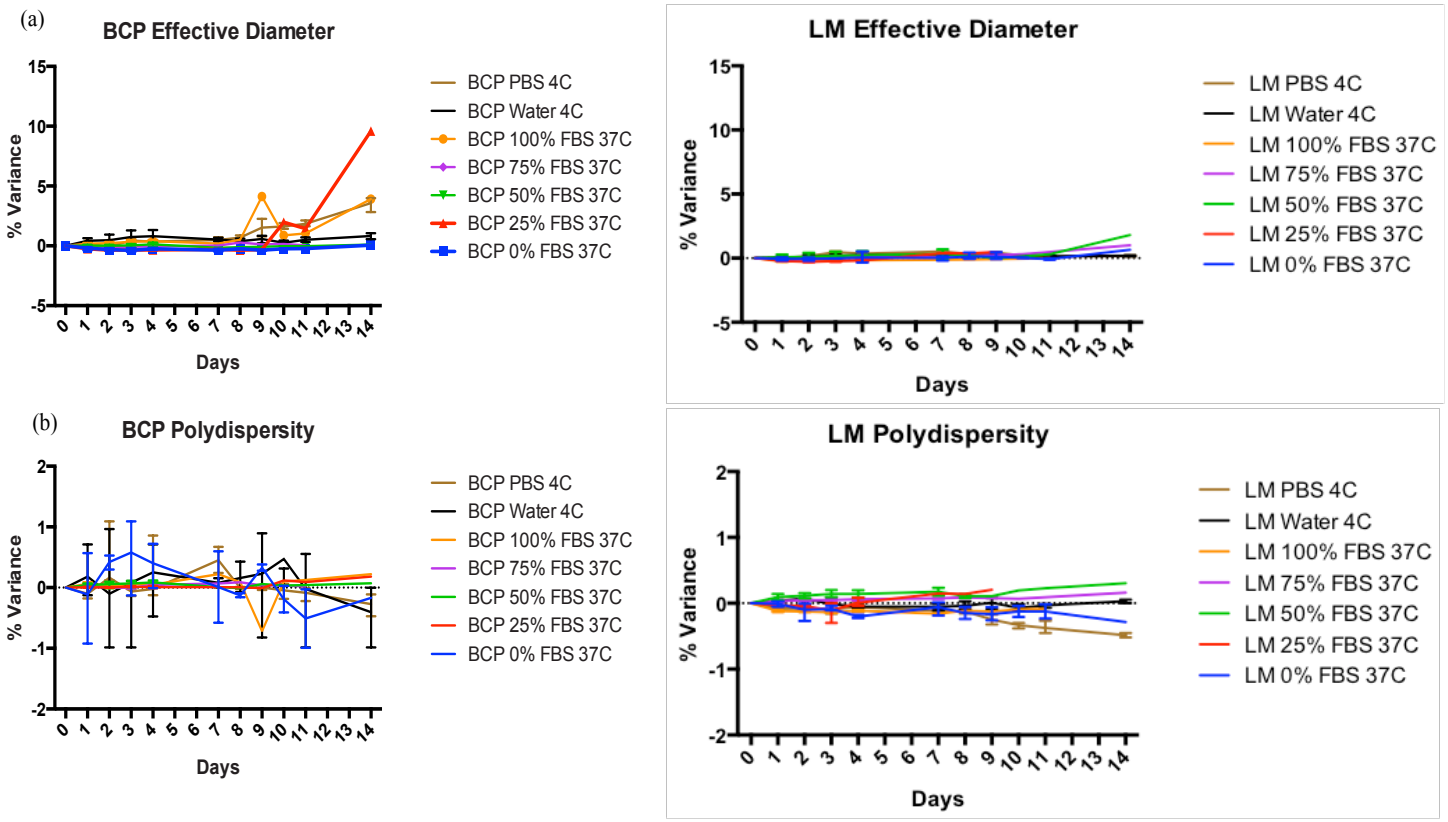

Figure 7: (a) BCP effective diameter in percent variance from time 0. (b) BCP polydispersity in percent variance from time 0. (c) LM effective diameter in percent variance from time 0. (d) LM polydispersity in percent variance from time 0.

by transmission electron microscopy (TEM):

Lipid Micelle (LM) and Block Co-polymer (BCP) Formulation: For both nanoparticle formulations, TEM resulted in images which give an indication as to the structure, size, and uniformity of nanoparticles. Images were difficult to capture, as the nanoparticle solution was too highly concentrated for individual nanoparticle imaging. However, for imaging of sections of nanoparticles, the images taken were accurate. For the BCP formulation, size and uniformity were similar to that seen in DLS results. For the LM formulation, it would seem that the MSD mean size results reviewed in figure 4 were correct, as the size by TEM appeared to be around 10 nm. (Fig.5)

Characterization of chemical composition of nanoparticles

Drug loading efficiency:

Lipid Micelle (LM) and Block Co-polymer (BCP) Formulation: For both nanoparticle formulations, the drug extraction process to reveal staurosporine incorporation proved to be a successful method for analyzing final concentration of drug within the nanoparticles. The BCP formulation demonstrated an incorporation percentage ranging from 20-40% (based on multiple nanoparticle batch analyses). The LM formulation demonstrated an incorporation percentage of 75-80% of staurosporine during the microfluidics synthesis process. (Fig.6)

Biodynamic properties of nanoparticles

Nanoparticle stability in water, PBS, and blood serum at 4ºC and 37ºC:

Lipid Micelle (LM) and Block Co-polymer (BCP) Formulation: For both nanoparticle formulations, DLS results were analyzed as a percentage of variance from the time 0 measurement as different solvents (water, PBS, or FBS) result in inaccurate, but precise measurement due to different viscosities of the liquids between samples. The stability of the nanoparticles gives an indication as to efficiency of long-term storage as well as to structural stability within the bloodstream during delivery. Past the eight-day point, some samples began to vary. (Fig.7)

Drug release profiling of nanoparticles:

Lipid Micelle (LM) Formulation: The drug release profile for the LM formulation revealed that at 24 hours, only 40% of staurosporine had leaked from the nanoparticles. As it is not possible to analyze drug presence in real-time, the dialysis was only run for 24 hours. By the steady drug release results achieved, one could extrapolate that the total load of staurosporine would likely be released by the 2-3 day mark. However, as per in vivo speculation, it would seem that the current drug release pattern would result in a large enough concentration of staurosporine to effectively kill the cancerous tumor once the cancerous site was reached by the nanoparticles. (Fig. 8)

In Vitro Analysis of Nanoparticle Cytotoxicity and Endocytosis

In vitro cytotoxicity assay:

Lipid Micelle (LM) Formulation: The lipid micelle formulation showed both low nano-carrier toxicity and a high drug-carrying capacity. At its highest concentration, a single dose induced cell death of around 70%, only a bit lower than that of free staurosporine. This indicates that the inclusion of staurosporine in the nanoparticle does not in any way cause a reduction in cytotoxicity of the

drug.

Block Co-Polymer (BCP) Formulation: The block co-polymer formulation also showed low nano-carrier toxicity but a lower drug-carrying capacity in terms of staurosporine inclusion. Even with a lower concentration of staurosporine per nanoparticle, and therefore a higher dosage of nanoparticle formulation required to reach a desired staurosporine concentration, at the highest concentration, the nanoparticle dosage still induced apoptosis of 70% of the cancer cells, only a bit lower than that of free staurosporine. This again indicates that staurosporine is still incredibly cytotoxic even when encapsulated within the nanoparticles.

In vitro nanoparticle lipid cancer cell integration confirmation:

Lipid Micelle (LM) Formulation: By imaging rhodamine, a die that is conjugated to 1% of the total lipid composition of the lipid micelle formulation, it was observed that cancer cells were recognizing nanoparticle lipids as their own, and subsequently integrating them into the cell membrane.

In vitro endocytosis confirmation by fluorescent microscopy:

For both formulations, the derived fluorescent microscopy images serve as an indication of nanoparticle uptake and subsequent nanoparticle load within cancer cells.

Block Co-polymer (BCP) Formulation: For the BCP formulation, the blue indicates cancer cell morphology, while the red/pink indicates the cy5.5 die or the uptake of BCP nanoparticles.

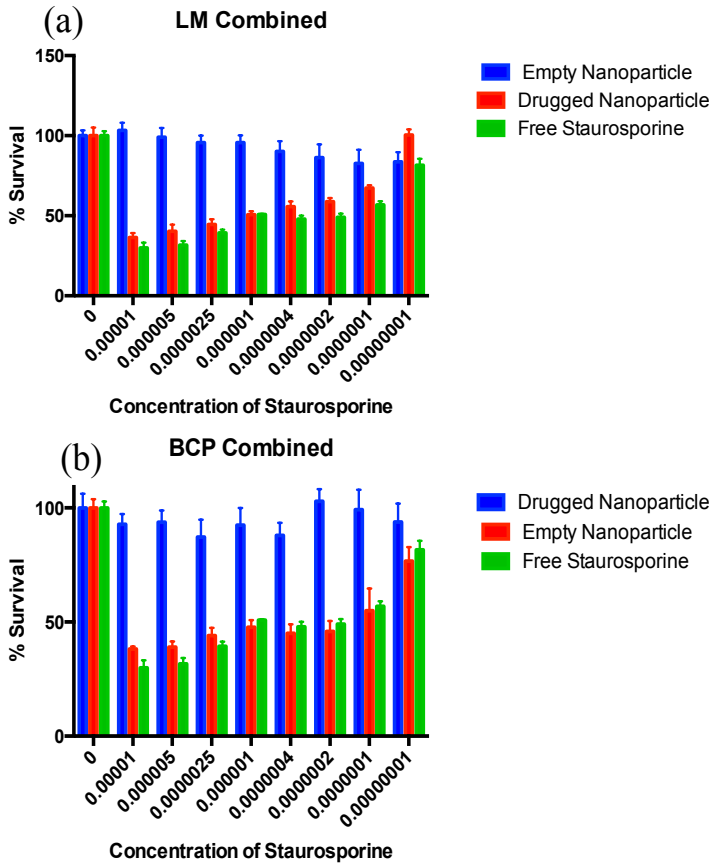

Figure 9: (a) MTT Assay results for LM formulation, which includes analysis of free staurosporine, empty LM nanoparticles, and staurosorine-loaded LM nanoparticles. (b) MTT Assay results for BCP formulation, which includes analysis of free staurosporine, empty BCP nanoparticles, and staurosporine-loaded BCP nanoparticles

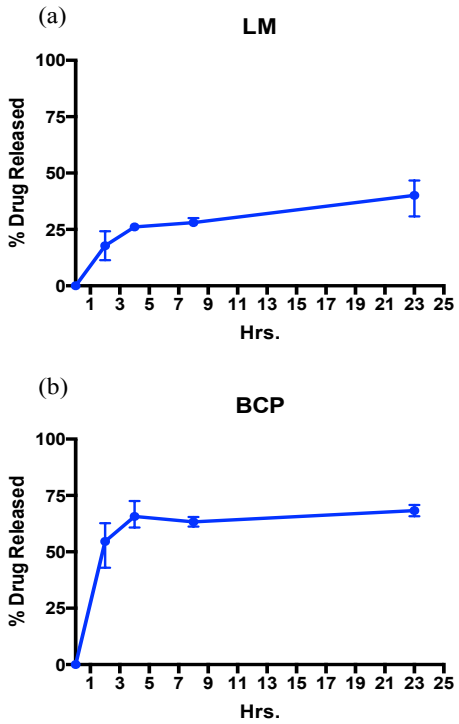

Figure 8: (a) Drug release profile for LM formulations. (b) Drug release profile for BCP formulationv

Lipid Micelle (LM) Formulation: For the LM formulation, the blue indicates cancer cell morphology, while the green indicates DIR dye or nanoparticle uptake.

Discussion

The development, characteristics, and in vitro analysis of these two nanoparticle formulations, have revealed that both nanoparticle platforms have the possibility to be used in the treatment and imaging of solid cancerous masses. The materials and methods of nanoparticle synthesis were easily purchased (with the exception of staurosporine, due to its rarity of being used) suggesting that the commercial production of these nanoparticles is feasible and cost-effective. The actual synthesis of a 2ml highly concentrated batch of nanoparticles can be performed in less than three hours, while subsequent analysis of basic structure (DLS, TEM, and drug incorporation) can be completed in less than two days. This process takes a much shorter time compared to nanoprecipitation and lipid-film hydration synthesis methods which not only translates to an ability to synthesize large batches quickly, but conceivably could also lead to a more efficient large-scale pharmaceutical production process (lower cost, less staff, etc.) Subsequent analysis of nanoparticle size revealed both formulations to be within the range for cancer-cell vascular morphology uptake via the EPR effect (15-100 nm +/- 5). Relatively low polydispersity also indicates that uniformity in nanoparticle size within the batch will allow injected nanoparticles to act in a similar way with each other, which should lead to the greatest nanoparticle uptake into cancer clusters. Analysis of stability of the nanoparticles for both long term storage, and as they are within the body reveal, that both formulations have a rigid structure which allows for extremely long storage and circulation

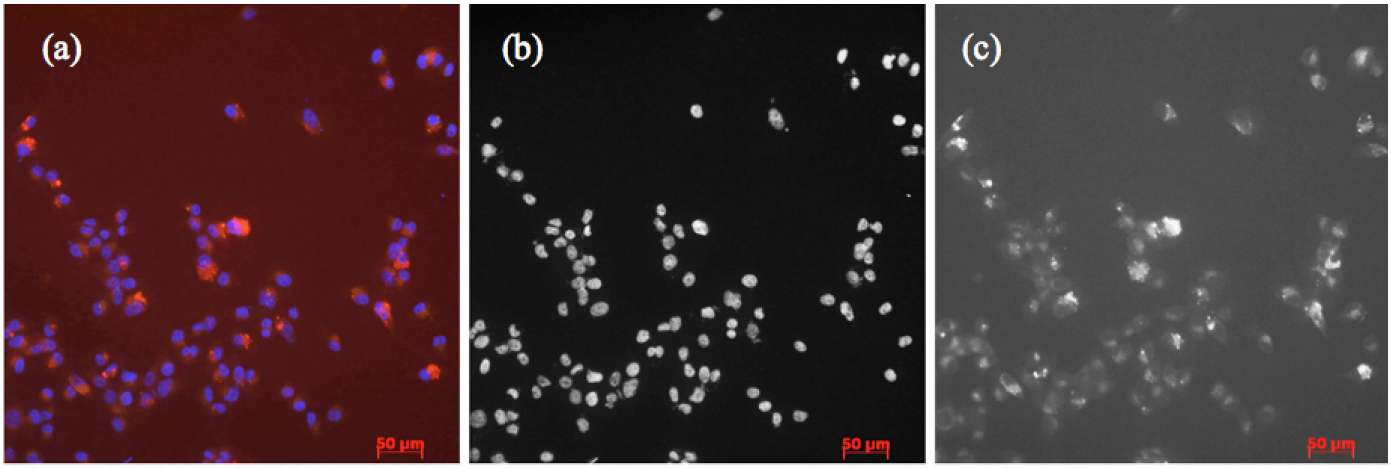

Figure 10: (a) Combined Image. (b) Cancer cell morphology. (c) Rhodamine imaging on cell membrane.

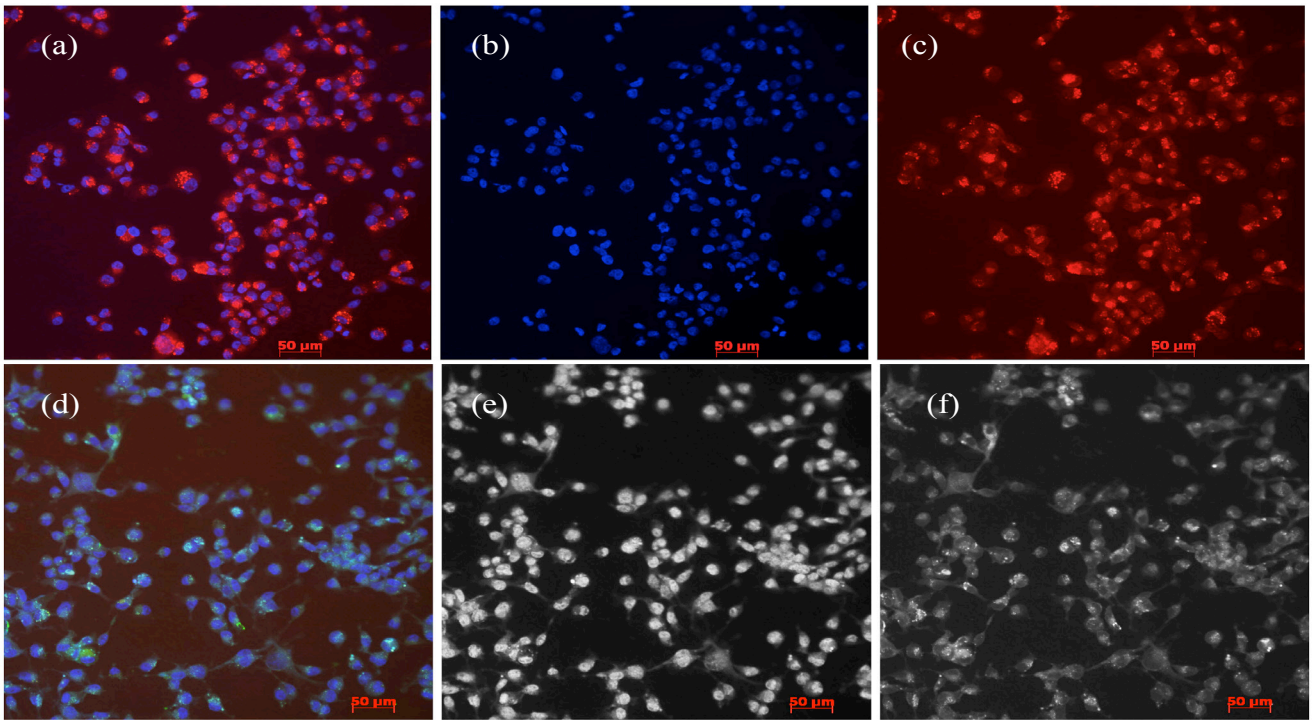

Figure 11: (a) BCP combination image. (b) BCP cancer cell morphology. (c) BCP cy5.5 nanoparticle load/uptake. (d) LM combination image. (e) LM cancer cell morphology. (f) LM DIR nanoparticle load/uptake.

within the blood-stream. Also, the process by which the nanoparticles' incorporated-staurosporine was quantified, serves as a model method for the analysis of staurosporine concentration within the nanoparticle solution, a protocol that will be critical for the preparation of patient doses. While the incorporation of staurosporine within the BCP formulation was significantly lower than that of the LM formulation, the resulting concentration necessary to attain the same concentration was still extremely aqueous, not reaching the "sludge" phase, which makes nanoparticles too hard to circulate in vivo. The profiling of drug release for both nanoparticles suggests that in an in vivo model, nanoparticles will have ample time to reach the tumor site and still have enough staurosporine within their core to be effectively cytotoxic to cancer cells. The analysis of cytotoxicity when introduced to cancer cells in vitro, suggests that within an in vvivo model nanoparticles which reach the cancerous site will go through either endocytosis or macropinocytosis, both of which result in cell-death. The images retrieved from fluorescent microscopy demonstrate that nanoparticles are going through endocytosis, and that while both nanoparticles are stealthy and unrecognizable to the body's various immune methods, the LM formulation is so inconspicuous that cancer cells recognize nanoparticle lipids as their own compounds, and integrate these lipids into the cell membrane, while simultaneously depleting the nanoparticles' core-contents into the cytoplasm of the cancer cell. This is perhaps one of the most persuasive demonstrations of the efficiency and promise of nano-biotechnology as a method for drug delivery, as this technique allows for direct and controlled interaction of designed drug formulation and desired molecular processes. Fluorescent microscopy methods also revealed the practicality of the included dies as a method for live

Mentor: Dr. Willem Mulder, Ph.D.

Associate Professor in Radiology Department, Mount Sinai School of Medicine.
We are very grateful for the dedication of the entire Nanomedicine group at the Translational and Molecular Imaging Institute.

MRI imaging of nanoparticles in an in vivo model, which can be used as a tool for tracking injected nanoparticles, imaging and identifying metastases and cancer clusters, and confirming cell-death with a post-treatment biopsy. The in vitro analysis and characterization of these two promising nanoparticle formulations has resulted in ample data to perform an in vivo study (which was not able to be completed due to the age of the researcher, who is under the age of 18, and therefore cannot perform research on animals as per IRB and IACUC regulations). Hopefully, future in vivo analysis will reveal tumor shrinkage and destruction, as well as an indication as to which of these nanoparticle formulations, or a mixture of these formulations is most effective as a cancer treatment, and therefore should be adapted to the human model.

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The Effects of Mindfulness-Meditation Practice on Anxiety levels Among High School Students, by Jordan Hudock, INTEL STS Paper excerpt.

Abstract

A shocking ninety-seven percent of college students report that they experience anxiety on a daily basis (Millar, 2010). Study after study shows meditation to significantly alleviate anxiety symptoms (Orme-Johnson et. al, 2013). This study sought to determine whether such alleviation would show up when average high school students participated in mindfulness meditation. Students' anxiety levels were assessed through the HAM-A scale directly before and after meditation sessions for three weeks. The collected data showed an average decrease in anxiety after meditation throughout the students and individual student progress in alleviating anxiety symptoms with increased exposure to meditation.

Hypothesis

Participation of high school student in mindfulness vmeditation practice will reduce the average level of anxiety in students.

Introduction

With the nonstop, always on the go, modern lifestyle almost all of us face, everyday anxiety has become an epidemic. In America, reportedly seventy-seven percent of all people are not able to cope with this stress or manage it in their daily lives (Millar, 2010). An even more shocking ninety-seven percent of college students report that they experience anxiety on

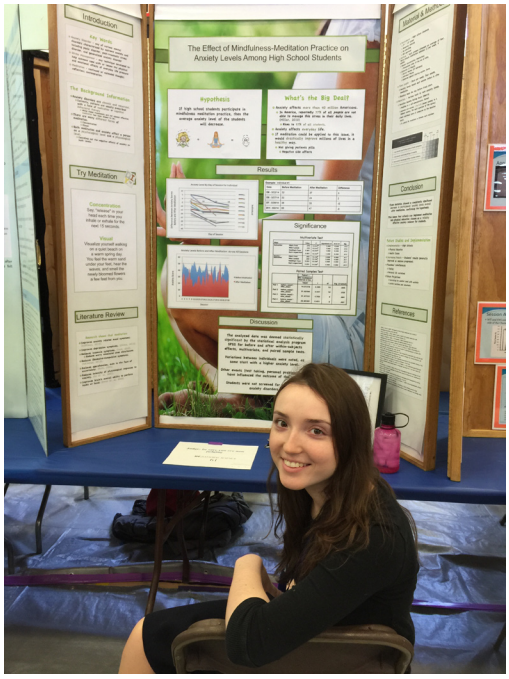
a daily basis as described in the same study (Millar, 2010). If something beneficial, not only to the students' stress levels, but also to their concentration and awareness levels, could be implemented in school systems, shouldn't it be? Study after study shows meditation to significantly alleviate anxiety symptoms (Orme-Johnson et. al, 2013) along with a reduction in sleepiness throughout the day and an increase in focus and awareness (Lee et. al, 2007).

Although multiple studies that document meditation's effect on anxiety have been published in recent years, not one has looked at meditation's effect on anxiety in those without noted anxiety disorders in a high school setting. This research is vital to the advancement of knowledge on how meditation affects anxiety because it focuses on our country's students, those with the highest reported levels of anxiety in America, and tackles the issue of anxiety in that entire population, never singling out those with diagnosed anxiety disorders.

Anxiety levels can be classified using psychological, physiological, or biological responses or lack thereof. When a person is experiencing anxiety, psychological responses include feelings of worry, nervousness, or unease, typically about an impending event or something with an uncertain outcome (Roth, 1994). Key examples of physiological response to anxiety include a lack of focus, an inability to unconsciously remain still, rapid breathing, trembling hands, cold hands and feet, a rapid heartbeat, a dry mouth and overall restlessness (So et. al, 2001).

During periods of anxiety, the muscle demands higher levels of glucose and oxygen running through the bloodstream. For this to be possible the heart has to pump faster and blood pressure must increase. The entire process starts when sensory cells alert the hypothalamus of a potential danger. Cells in the hypothalamus transmit a signal to the pituitary gland, which releases the adrenocorticotropic hormone (ACTH) to the adrenal glands (So et. al, 2001). ACTH signals to both adrenal glands to produce more cortisol. ACTH molecules bind to receptors on the surface of adrenal cells, which initiates a complex process that turns cholesterol into cortisol. When produced, this hormone is pumped into the body and attaches to its receptors. At this point, cortisol can interact with other cells to increase the sensitivity of the heart and blood vessels. This leads to the effects of epinephrine and norepinephrine. These hormones stimulate receptors in heart cells, which increase the rate of the heartbeat and the force with which the heart muscles contract (Shapiro et. al, 2008). Cortisol also ensures that the blood vessels are receptive to epinephrine and norepinephrine. These hormones attach to specific proteins, which cause the narrowing of blood vessel walls. This brings about an increase in blood pressure and allows blood to be sent to essential organs and muscles.

Meditation is commonly associated with reducing the symptoms of anxiety. It is a form of contemplation, reflection, or heightened awareness. Alterations in brain function during meditation have been recorded using single photon emission computed tomography, electrophysiology, PET and functional magnetic resonance imaging (Travis, 2001). Although results differ slightly betweenforms of meditation, overall results indicate intensified signals in brain regions related to attention control and affect regulation, with an increase in dopamine release.



One study, entitled Effects of Transcendental Meditation practice on brain functioning and anxiety reactivity in college students, was executed to determine the effects transcendental meditation practice had on brain function and anxiety levels in college students (Oman et. al, 2008). This trial investigated the effects of Transcendental Meditation (TM) on broadband frontal coherence, preparatory brain responses, and power ratios, all of which were measured using the Brain Integration Scale. Fifty college students participated in a pretest, then were assigned to learn either TM immediately or after a ten-week posttest. Analyses revealed significant increases in Scale scores for students who began learning TM immediately, but decreases in students whose learning was delayed. There were significant reductions in sleepiness among immediate-start students with no change in delayed-start students. The trial showed no changes in habituation rates in immediate-start students, but significant increases in delayed-start students. These data support the value of TM practice for college students and, therefore, it would be interesting to research whether or not these effects translate into benefits for high school students, the subjects of this study.

Another study, done in 2007, was focused on determining the effects that meditation practice had on brain function and anxiety levels in participants diagnosed with anxiety compared to healthy participants (Lee et. al, 2007). During this trial, forty-eight participants with anxiety disorder were assigned randomly to either an eight-week meditation program or an eight-week education course. Those in the meditation group practiced meditation over that period of time while the education was instructed on how one should respond to one's anxiety. Results were measured every other week using the Hamilton Anxiety Rating Scale (HAM-A), the Hamilton Depression Rating Scale (HAM-D), the State–Trait Anxiety Inventory (STAI), the Beck Depression Inventory, and the Symptom Checklist-90—Revised (SCL-90 -R[U1]). This study's

results show a larger decrease in anxiety within the mediation group than the education group, the therefore supporting this paper's hypothesis that meditation is an effective alleviator of anxiety symptoms. The results also show an increase in attentiveness among meditation-group participants.

A third study that specifically demonstrates this paper's hypothesis is called: Randomized trial of a meditation-based stress reduction program and cognitive behavior therapy in generalized social anxiety disorder (Koszicki et. al, 2007). Its trials sought to see how well meditation worked in anxiety compared with established psychotherapy interventions. Fifty-three patients diagnosed with generalized social anxiety disorder participated in either and eight-week meditation program or twelve sessions of group therapy targeted at the disorder. The meditation group showed significant improvement in their self-measured anxiety at the end of the trial period, supporting the hypothesis that meditation could be used to alleviate symptoms of anxiety among high school students.

Various studies were done to support the theory that meditation significantly reduces anxiety levels. One such example is a recent study by Richard Davidson and colleagues (Davidson et. al, 2013). This study was based on the research that opening oneself up to rather than resisting possibly painful experiences can actually steer one's mind away from anxiety. Being open to these types of experiences is a documented result of meditation. For this reason, Davidson sought to discover whether or not meditation would steer peoples' minds from stress in this way. During this study, functional magnetic resonance imaging (fMRI) was used in meditators to dissociate neural activation patterns linked with pain. Compared to non-meditators, meditators experienced significantly less unpleasantness.

Anxiety is extremely prevalent in school systems and meditation is a potential tool that could be used to alleviate symptoms. Schools could take a few minutes each day to integrate meditation into classes in productive ways. As demonstrated in the above four studies, this would likely lower the anxiety levels of students and improve their abilities to concentrate and think clearly throughout the day.

This paper investigates the role mindfulness-meditation practice plays in alleviating anxiety symptoms among high school students. It is hypothesized that participation of high school students in mindfulness meditation practice will decrease the students' average anxiety level. The above four literature reviews exhibit and support that hypothesis. This study will differ from the directly above-mentioned involving college students (Oman et. al, 2008) because, with high schools students, there is an age difference, difference in maturity level, difference in the pressures students face (social and educational), among other variables. (...)

Fig 1: Before and After Test Within-Subjects Effects

Source		Sig.
BeforeAfter	Sphericity Assumed	.012
	Greenhouse-Geisser	.012
	Huynh-Feldt	.012
	Lower-bound	.012

Results

Each individual was given a number (#1 - #11) and participated in 2 - 4 separate meditation sessions. The differing number of sessions between students can be attributed to the study being conducting at the end of the school year where scheduling became less consistent in terms of finals and off-days. Since most students only have gym every other day, some ended up having more gym classes than others because of how such scheduling interfered with their gym days. In total, data for 39 sessions were

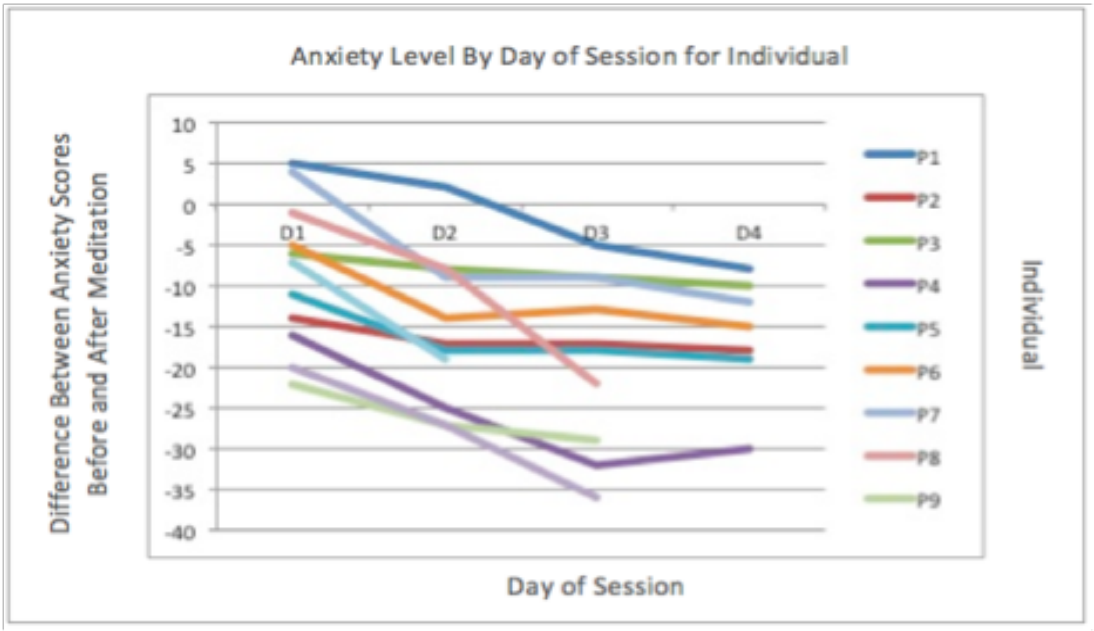
Fig 2: Paired sample tests

		Paired ... 95% Confidence Interval of the ... Upper	t	df	Sig. (2-tailed)
Pair 1	before_sess1 - after_sess1	14.51310	2.295	10	.045
Pair 2	before_sess2 - after_sess2	21.02706	2.531	10	.030
Pair 3	before_sess3 - after_sess3	21.97725	4.763	9	.001
Pair 4	before_sess4 - after_sess4	23.95165	5.651	6	.001

Fig 3: Multivariate Test

Effect		Value	F	Hypothesis df	Error df	Sig.
BeforeAfter	Pillai's Trace	.676	12.547[b]	1.000	6.000	.012
	Wilks' Lambda	.324	12.547[b]	1.000	6.000	.012
	Hotelling's Trace	2.091	12.547[b]	1.000	6.000	.012
	Roy's Largest Root	2.091	12.547[b]	1.000	6.000	.012
Session * BeforeAfter	Pillai's Trace	.902	12.338[b]	3.000	4.000	.017
	Wilks' Lambda	.098	12.338[b]	3.000	4.000	.017
	Hotelling's Trace	9.253	12.338[b]	3.000	4.000	.017
	Roy's Largest Root	9.253	12.338[b]	3.000	4.000	.017

Figure 4



collected. For each session, a score for a subject's anxiety before meditation and a score for his or her anxiety after meditation was collected. The lowest score a subject could receive was a 12 and the highest was a 60 based on the range of the scale and the number of questions. A higher score represents a higher level anxiety while a lower score represents a lower level of anxiety. After all such score sets were collected, the difference in anxiety before and after meditation was calculated for each.

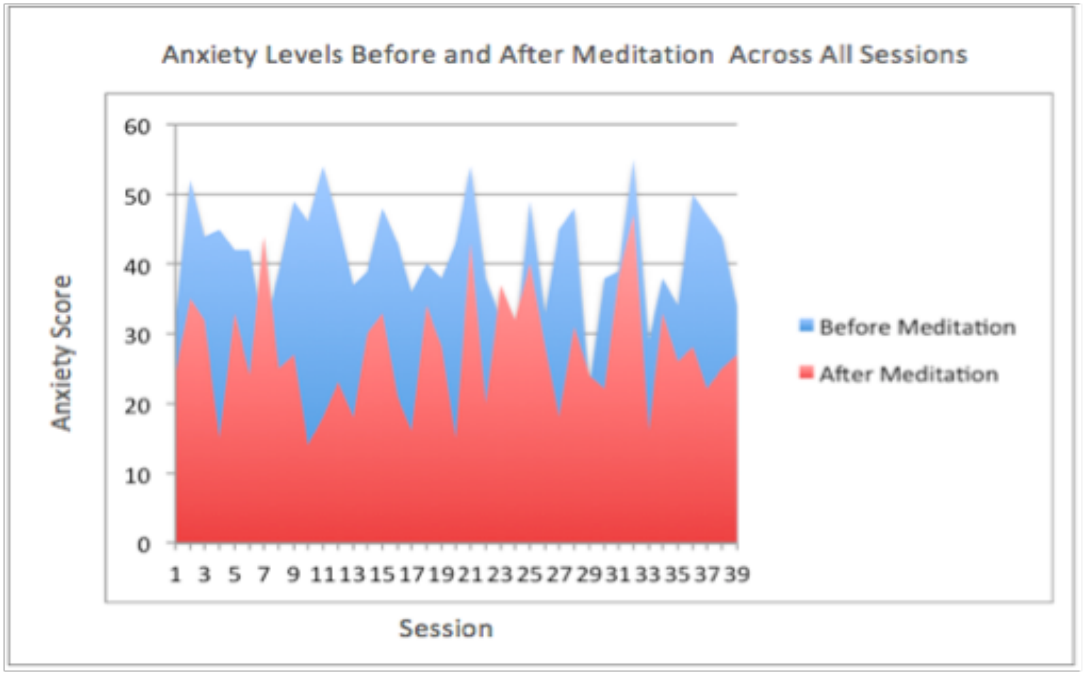
We ran a variety of statistical tests on the above data including paired samples tests, multivariate tests, Mauchly's test of sphericity, tests of within-subject effects, and tests of between-subject effects. We used such a wide range of tests to try and get the most accurate information possible by comparing results of each test. The analyzed data was deemed statistically significant by the statistical analyzation program SPSS for before and after within-subjects effects, (Fig. 1), paired sample tests (Fig. 2) and multivariate (Fig. 3).

The above tells us that there was a consistently significant decrease in participants' anxiety levels after meditation as the hypothesis predicted. Visual representations of anxiety level by day of session for individual participants and anxiety levels before and after meditation across all sessions are shown in Figure 4. The difference in anxiety scores between before and after meditation scores consistently decrease. This suggests that individuals become increasingly better as they practice meditation more. The decrease in difference could, however, be attributed to other factors such as participants becoming gradually more comfortable with the session environment. The graph in Figure 5 shows how anxiety scores for subjects across all sessions after meditation were almost totally consistently lower than anxiety scores for subjects before meditation.

Discussion

The significance of this data means that schools can implement meditation into physical education classes as a reliably effective anxiety reliever for students. As expected, the scores students' anxiety reduced to after meditation depended on each individual's anxiety level before meditation; if his or her initial anxiety level was especially high to start with, their anxiety level after meditation would not be as low as someone whose initial anxiety was lower. The amount these levels reduced (the difference between a subject's anxiety level before and after meditation), however, varied not according to initial anxiety level but by individual. This could be attributed to a range of factors from a subject's mindset about meditation and its effectiveness to the turmoil or lack thereof occurring in a subject's life at the time of their meditation sessions. A pattern did arise, however, in students' improvement in meditation throughout multiple sessions. Nearly consistently, the difference in students' anxiety levels before and after medita-

Figure 5



tion grew significantly in their first few sessions then began to level out by their third or fourth day practicing meditation. Students also seemed to improve with practice (the absolute value of their average differences seemed to rise the more days they participated). For instance, individual #10's difference between his or her before and after meditation scores D0 was -20. On D2 the difference was -27 and on D8 it was -36.

As mentioned in the results section, the growth in the absolute value of the difference between students' anxiety levels before and after meditation could be attributed to them simply improving in meditation as they got more used to it. The leveling out of this growth toward later sessions could be attributed to multiple causes such as complacency or difficulty remaining focused when hearing the same meditation tracks over again. To account for this possibility, it would be interesting to conduct a study in which a different meditation tracks was used each session. Although the decrease in anxiety was proved to be statistically significant, a study needs to be done that controls for a placebo effect. Anxiety levels could, for instance, be decreasing simply because participants' "before" meditation scores were affected by their previous class and getting out of that stressful environment alone lowered anxiety. To control for placebo effect, it would be helpful to conduct a follow-up study that compared average high school students who did meditation to those who did another simple activity such as drawing. Creating such a control group was not possible in this study due to limited facilities and volunteers.

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Human Facial Recognition by Pigeons (Columbidae), by Jane Milcetic (Junior)

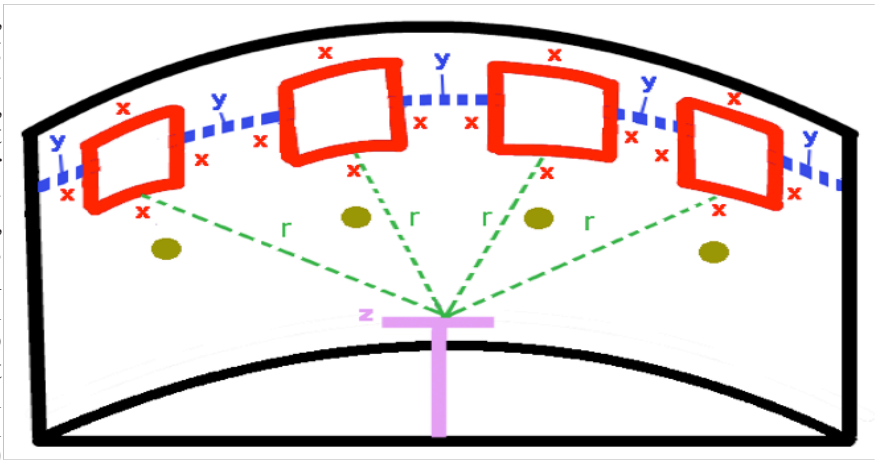
Until recently, the capabilities of the avian brain have been underestimated. Modern studies now focus on the astounding competence of the previously underrated species (Happ, 2013). Facial recognition, a skill thought to be specific to humans, seems to be possessed by some birds as well (Soto, 2011). Corvids, pigeons, and other fowl with high brain to body ratios have been able to identify human faces from one another, based on the bird's preference of discrimination (Bhatt , 1988; Bogale, 2010; Soto, 2011). Despite the building amount of research investigating the reason as to why birds can tell two people from one another based on their facial features, much is still unknown about the extent of this ability and its anatomical basis.

Birds have been discredited for their intelligence due to Ludwig Edinger's assumption in the 1800's that the avian brain had no gyri, leading other scientists to be disinterested with the supposedly primitive species (Happ, 2013). Edinger reasoned that the wrinkle-free brain indicated that birds relied on instinct rather than processing thoughts and acting upon them (Happ, 2013). Past the barrier of supposition, the comparison of the human and the bird brain shown that they have similarities in functions, yet a different anatomical organization (Happ, 2013; University of California Tele-

vision, 2008). The pallium exemplifies this, it being the outer layer of the brain in all vertebrates that has sections with functions specific to the species (Weiner, 2013). Marzluff, Miyaoka, Minoshima and Cross found that when American crows (Corvus brachyrhynchos) viewed familiar human faces, their mesopallium and nidopallium activated (Marzluff, 2012). The mesopallium is used for imprinting, memorizing and recognizing birdsongs, while the nidopallium makes decisions (Weiner, 2013). Their discoveries shed more light on the enigmatic topic of avian neurology.

Posamentier and Abdi traced facial recognition in humans to the occipital gyri, the fusiform gyri, and the superior temporal sulcus (Posamentir, 2003). More developed in their definitions, they credit the occipital gyri with memorizing the basic form of facial features and their variations, the fusiform gyri with remembering unchanging facial features, and the superior temporal sulcus with perceiving emotion through observation of expression and motion. Shared by both the avian brain and the primate brain is the striatum, which is involved with learning and movement (Marzluff, 2012). The memory system sends signals between other components of the brain to store information, and interacts with the prefrontal cortex, the human version of the nidopallium (Weiner, 2013). Through the parallelism of the human and avian brain, more can be discovered about the latter, and even some about the former.

Bhatt, Wasserman, Reynolds and Knauss tested 8 feral pigeons on their ability to classify objects in the natural or manmade category (Bhatt, 1988). Using pictures of humans, cats, cars, and chairs that differed in their setting, visibility, orientation, et cetera, 8 birds were trained to identify an image in two ways. Since it has been proven that pigeons can memorize 200 slides if not more, Bhatt, Wasserman, Reynolds and Knauss designed an experiment to test if their subjects were memorizing the 40 presented pictures, or relied on fitting the photograph into the four categories. Out of 2,000 slides, 40 images were chosen to be the familiar group, 10 for humans, 10 for cars, and so on. On uneven days, the familiar group was shown, while a new set of 40 pictures, each category represented by ten photos, was shown on the even days. The unfamiliar images were chosen from the remaining 1,960 slides. After 96 days, the pigeons finished their testing. While the subjects struggled with the non repeating photos, every bird's scores were above chance level. The highest scores in the repeating category were at 91%, and the lowest were at 20%. The highest scores in the non-repeating category were at 84%, and the lowest were at 19%. Since some pigeons succeeded at discriminating between images, though others lowered the statistics, as they lacked the competence to complete the task. The experiment was done another 3 times, each with the same subjects, though the 40 pictures in the familiar group were changed to ensure that the birds' scores were not affected by an odd image. Out of the 4 trials, the pigeons maintained relatively consistent percentages, supposing that each subject had their own way of telling one category apart from another. It seemed that the birds were objectifying the humans, as they viewed still slides, and not moving pictures (Bhatt, 1988). While humans are able to recognize another person as a being and not an item, it is unclear how pigeons categorize people, not just pictures of them. A study by Marzluff, Miyaoka, Minoshima and Cross study leads to the idea that the parts of the avian brain may have undiscovered features that allows them to memorize the face of person and use it to their advantage (Marzluff, 2012).



Gibson, Wasserman, Gosselin and Schyns tested 4 pigeons using colored photographs of 32 faces to see if the birds could categorize the stimuli, as well as what facial features and areas they used (Gibson, 2005). The subjects were trained to recognize either emotion or gender until they could categorize 32 plain faces and two partially occluded faces with 70% accuracy. Then, the same faces were blotted with "bubbles", computer-generated grey splotches that concealed parts of the face. The pigeons viewed 320 bubbled faces in a block, and performed 7 blocks per day. Each of the 32 faces had its own percentage of how often the subjects correctly selected it, as did each bird. The final results showed the two in the emotional category scored 91% and 75%, while the gender category scored 71% and 85%. Faces that had the chin uncovered led to those in the emotion group to select correctly, while a revealed mouth aided those in the gender group to determine the sex of the target. Bogale, Aoyama, and Sugita studied a similar concept with 6 jungle crows, evenly split between determining either if the photo face was male or female (Bogale, 2010). After each bird reached 80% correct with the regular photographs that showed men and women sans hair (eyebrows were kept) from the middle of the neck up,

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the images were altered by making it colorless, contouring the face, or barring out certain features. When the pictures were greyed, the subjects gravitated towards the mouth and the eyes, indicating that the crows relied on color (particularly the hue of the pupils, and the jaw and chin region). These scientists suggest that crows may remember faces to obtain food, maintain dominance, and ward off unwelcome humans (Bogale, 2010). Urbanization is also pressing factor that forces birds to live with humans, and adapt to the new way of life. Since a bird must account for its predators, remembering a human face could save its life.

While the aforementioned studies delved into the foreign subject of the avian brain using methods to determine if birds can use faces to discriminate between people, few have investigated how they do this. The use of MRI machines to view the areas of the bird brain is difficult, as the subjects constantly move, and sedatives hinder cognition. Even though chances of picturing the avian brain are slim, the use of motion incorporated in an experiment could improve the perception of the species. While most studies have used still photographs, thus creating the possibility that birds memorize the face as an object rather than a living thing (Bhatt, 1988). The use of repetitive training could result in birds telling one human apart from another (Bhatt 1988), though a mechanism in the avian brain could be responsible for their abilities.

Rarely are pigeons tested on their capacity to recognize living human faces in a lab setting. The previous experiments had too little control of how the pigeons viewed the faces, either causing ruptures in the recognition process, or causing objectification of the human (Bhatt 1988, Soto 2011, Dittrich 2010). The first step to avoiding these errors is to introduce human subjects that are viewed from consistent angles, vertical and horizontal distances, and lighting designs. A semicircle testing area with 4 windows, each the same size, and equidistant from one another, would frame the faces while keeping them at an equal radian's length away from the pigeon, who would sit at the center. While the pigeon would sit inside the semicircle enclosure, the people would stand outside, only their faces visible through the window. A modified hood would cover the people's necks and hair, leaving only the area from the forehead to the chin visible. To reveal the faces at the same time, blinds would be installed outside of the semicircle. Inside, one button below each window would enable the pigeon to receive an edible reward after flying and pecking it.

In order for the pigeons to grasp how the reward system works, they must be conditioned through pretraining. When the bird is on the perch, a constant person (CP) will be revealed by raising the blinds. Even in pretraining, the pigeons will be separated into two groups, Group 1 and Group 2. Each of these groups has a different CP, referred to as CP1 or CP2. CP1 and CP2. The two constant persons, CP1 and CP2, will have a similar age range, race, and sex, as will all other people used as stimuli. Only two pigeons will be in Group 1 and Group 2 to make sure that the face of either CP will have little or no effect on the results. To ensure that the pigeon remembers its CP, only the button beneath the window that the CP stands in will activate when pushed and administer food. Until all pigeons reach 75% accuracy, every pigeon will continue pretraining with its CP. If some pigeons cannot reach 75% accuracy within a reasonable amount of time (to be determined), those pigeons will be rejected from the experiment.

The data for the experiment will be collected through a process relatively similar to the pretraining. Again, the pigeon will sit on its perch and wait for the stimuli to be unveiled. Four faces will appear this time, one of them the pigeon's CP. As in the pretraining, the pigeon will fly to whichever window and peck the button underneath. This time, all buttons will activate, but only the CP's will reward the pigeon. The whole process will repeat, and the CP will change the window it stands in every trial. Three new people will fill in the spots every trial, never having a repeating non-constant person. This will allow the pigeon to solely focus and memorize the CP

Procuring the extent to which pigeons can identify human faces offers more information about the avian brain, as well as the human brain. The tectofugal visual pathway in the pigeon brain, which is suspected to be involved with the interpretation of human faces, is related to the pulvinar in humans (Husband 2001). By measuring the performance of the tectofugal pathway in this discrimination trail, the secondary visual system of human can be further understood. This could have a critical role in restoring some visual abilities in people whose primary visual system does not activate due to a stroke or other similar accidents.

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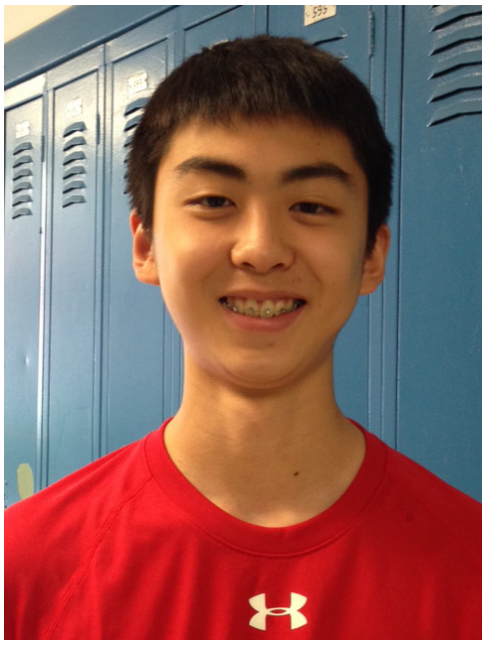
Altered Gastrointestinal and Immunological Profiles in Children with Autism Spectrum Disorder (ASD), by Jonathan Chung (Sophomore)



Autism Spectrum Disorder (ASD) is a neurodevelopmental condition that is diagnosed based on behavioral symptoms such as impaired communication and repetitive behavior (Ashwood et al; 2010). Between individuals, the severity of these core behavioral symptoms can drastically differ hence giving its name of "Spectrum" (Ashwood et al; 2010). This spectrum refers to the heterogeneity observed across individuals with ASD (Ashwood et al; 2010). For instance, there are a multitude of possibilities for the underlying causes of this disease and the developmental manifestations (Ashwood et al; 2010). Some of the most significant differences between individuals lie in the array of non-neurological comorbidities that subsets of individuals suffer from (Capuron and Miller 2011). Specifically, gastrointestinal abnormalities, suffered by 7 out of 11 ASD children, and immune dysregulation prove to be of particular importance (Capuron and Miller). These comorbidities provide insight into new pathways that can be used and manipulated to develop treatments and potential cures for ASD patients.

The notion of interactions between the brain and immune system has become the research field of psychoneuroimmunology (Capuron and Miller 2011). It has been suggested that the immune system can influence the brain and behavior through cytokine pathways, where cytokine signals actually reach the brain through cellular, neural and humoral pathways (Capuron and Miller 2011). Specifically, during inflammation, pro-inflammatory cytokines can access the central nervous system and interact with a cytokine network in the brain to influence almost every aspect of brain function relevant to behavior (Capuron and Miller 2011). This discovery explains how the administration of certain cytokines to human subjects causes changes in mental state (Ashwood et al; 2010). For example, increased plasma levels of IL-4 correlate with greater deficits in communication (Ashwood et al; 2010). Conversely, mental state such as chronic stress and depression can affect the immune system (Ashwood et al; 2010). Vulnerability factors such as age and obesity, work in conjunction with immune to brain signaling to worsen immunologic contributions to neuropsychiatric disease (Capuron and Miller 2011). For ASD, the altered immune system includes altered cytokine profiles in the postmortem brain, cerebrospinal fluid and plasma (Hsiao et al; 2012). In general, ASD children exhibit increased levels of proinflammatory cytokines and decreased levels of regulatory cytokines (Hsiao et al; 2012). Additionally, peripheral immune abnormalities such as altered serum Ig levels are apparent in children with ASD. These peripheral environmental conditions specific to ASD prove to be involved in the long-term programming of immune dysfunction (Hsiao et al; 2012). This was concluded by the result of irradiated control mice repopulated with bone marrow from MIA offspring not also translating over the MIA-related immunological deficits. To further reinforce this, MIA offspring who were irradiated and repopulated with normal bone marrow from control mice no longer demonstrated behaviors typical of ASD hinting that ASD-like behaviors result from the immune abnormalities in the MIA offspring (Hsiao et al; 2012).

There are an abundance of examples of immune dysregulation in ASD that can be observed in the brain, periphery and gastrointestinal tract (Capuron and Miller 2011). Among these is the observation that CD4+ cells from spleens of 15-wk-old MIA offspring release significantly more IL-6 and IL-7 compared to controls (Hsiao et al; 2012). These same results are recorded in 3 week old and 1-year-old offspring demonstrating an early onset of persistent immune dysfunction (Hsiao et al; 2012). In regard to the profile of peripheral immune cells, MIA offspring exhibit decreased levels of regulatory T cells, hyper-responsive CD4 T cells and elevated levels of Gr-1 cells.

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The observation of hyperresponsive CD4 T cells is of particular interest because it reflects diminished immune homeostasis (Hsiao et al; 2012). In a human study, significant increases in IL-1B, IL-6, IL-8, and IL-12p40 were observed in children with ASD compared to controls (Ashwood et al; 2010). Additionally, as certain cytokine levels increased, the impairments in behavior became more pronounced (Ashwood et al; 2010). ASD-inflammatory subtype children could have impaired regulation in steps of IL-1B production (Jyonouchi et al; 2014). Interestingly, dysregulated production of IL-1B and IL-6 leads to chronic inflammatory conditions of the CNS, joints and GI tracts (Jyonouchi et al; 2014). The involvement of the overproduction of IL-6 and IL-1B in the pathogenesis of juvenile idiopathic arthritis supports this claim (Jyonouchi et al; 2014).

The radical idea that a gut-brain axis may exist continues to gain support as current research continues. A main contributor to beginning this entire field of research was the fact that many mental illnesses such as autism, Rett syndrome and cerebral palsy have gastrointestinal issues as well. Additionally, children with these illnesses have different gut microbiota composition from neurotypical children (Hsaio et al; 2013). So far, there are many explanations about how this axis works but none that are universally accepted. Suggestions exist, such as the axis involving neuronal circuits, alterations in synaptic plasticity genes and the vagus nerve (Heijtz et al; 2011). However, it is likely that the gut-brain axis is a bidirectional homeostatic route of communication that uses neural, endocrine and immune pathways where the gastrointestinal tract provides the scaffold for these pathways (Cryan and Dinan 2012). This idea can provide the basis of new ways to prevent, diagnose, treat and potentially cure many neurological disorders (Kang et al; 2013).

An emerging idea is to use probiotic therapy, where probiotics are live organisms that stimulate the growth of other microorganisms, usually ones that provide beneficial properties to the host (Cryan and Dinan 2012). Normally, probiotic therapy is used to treat issues and illnesses related to the gut, but it could be used to treat neurological illnesses as well because of the gut-brain axis (Cryan and Dinan 2012). For example, the probiotic of Lactobacillus rhamnosus decreased anxiety and despair-like behavior and reduced stress-induced increase of plasma corticosterone levels in mice (Cryan and Dinan 2012). In this particular case this most likely occurred because the probiotic treatment altered the mRNA expression of GABA receptors in the central nervous system (Cryan and Dinan 2012). Another example is the probiotic agent Lactobacillus farciminis, because it prevented intestinal barrier leakiness and also reversed psychological stress (Cryan and Dinan 2012). However, this is no surprise because chronic stress is known to affect the gut microbiota composition and disrupt the intestinal barrier making it leaky thus allowing the increase of circulating levels of immunomodulatory bacterial cell wall components such as lipopolysaccharide (Cryan and Dinan 2012). The gut microbiota composition is very important because it determines health since a rich and diverse gut is a healthy one (Kang et al; 2013). Irritable Bowel Syndrome patients support this claim because they have 25% fewer genes in the gut than healthy controls (Kang et al; 2013). A higher diversity of gut bacteria allows better microbial integrity and the ability to protect the human intestine from environmental stresses including the intake of pathogenic gut microbes (Kang et al; 2013). When the gut microbiota diversity is low, then the gut is more susceptible to pathogens, which can disrupt the gut-brain axis causing pathophysiological consequences (Cryan and Dinan 2012). The gut microbiota composition can be manipulated through diet, infection, disease and antibiotics (Cryan and Dinan 2012). On the positive side, this allows probiotic therapy and antibiotic treatment to work and cure diseases and restore gut microbiota diversity (Kang et al; 2013). Additionally, it explains why some specific diets such as a gluten and casein free diet can improve symptoms of autism occasionally, and more specifically in the subset of ASD patients who have gastrointestinal disorders as well (Finegold et al; 2002). However, on the other hand, this ability to change the diversity of the gut microbiota allows a western-style diet and overuse of antibiotics at an early age to contribute to problems (Kang et al; 2013). Heijtz, 2011, demonstrates a strong piece of evidence supporting how the gut microbiota influences the brain. In this paper, specific pathogen free mice (SPF) have altered behavior from germ free (GF) mice, which is most likely due to their differences in gut microbiota. The germ free mice demonstrated increased motor activity and less anxiety-like behavior in comparison to specific pathogen free mice (Heijtz et al; 2011). However, when these germ free mice were exposed to gut microbiota in early life, they displayed a behavioral phenotype similar to the specific pathogen free mice (Heijtz et al; 2011). This scenario is extremely similar to how the maternal immune activation (MiA) model works. In the MIA model, infected mothers have a higher chance of having offspring with symptoms of autism (Hasio et al; 2013). Both instances occur because of developmental programming which says that early life environmental influences may impact an organism's later development, structure and function (Heijtz et al; 2011).

Autism is a neurodevelopmental disease that is most likely related to the gut-brain axis. It is diagnosed when people show signs in their behavior such as deficits in social interaction and language. Interestingly, at the onset of autism, gastrointestinal symptoms arise (Finegold et al; 2002), which include altered gastrointestinal motility and increased intestinal permeability (Hsiao et al; 2013). Additionally, significant alterations in the upper and lower intestinal flora of children occur at the onset of autism (Finegold et al; 2002). These alterations in the intestinal flora in autistic children induce changes in the intestinal gut microbiota as compared to neurotypical children (Cryan and Dinan 2012). This change in composition in autistic children is a loss of diversity, with lower levels of a group of distinctive bacterial genera (Kang et al; 2013). This less diverse and rich gut has negative correlation with gastrointestinal symptoms severity, reinforcing the idea that a healthy gut is a diverse one (Kang et al; 2013). Specifically, lower levels of the Prevotella genera were found to be most significant changes (Kang et al; 2013). It happens that the Prevotella genus is important in all gut microbiota composition. The Prevotella genus determines the gut-microbiome profile, and was proposed as one of the three main microbes characterizing the human gut microbiome (Kang et al; 2013). Since the Prevotella species have essential genes for the biosynthesis of vitamin B1, it also was reported to alleviate Autism Spectrum Disorder symptoms (Kang et al; 2013). Within the Prevotella genus, Prevotella copri, the most significant species in the Prevotella genus has different incidence in the gut microbiota composition of autistic children (Kang et al; 2013). When there is a loss of Prevotella copri-like microbiota in autistic samples, it could result in a major reconfiguration and reduced complexity in the intestinal microbial ecosystem (Kang et al; 2013). This loss could also contribute to the alteration of community-wide interrelationships in gut microbiota in autistic children (Kang et al; 2013). For example, neurotypical children have a negative correlation between Prevotella levels and Enterobacteriaceae while autistic children had no correlation given that both groups of bacteria were found at minimal levels (Kang et al; 2013). There are hypotheses that suggest a decrease in Prevotella and certain levels of species in general may be due to diet patterns (Kang et al; 2013). For example, a high carbohydrate-based diet shifts the intestinal microbiota towards the Prevotella-rich enterotype (Kang et al; 2013).

Another hypothesis for the causes of autism from the gut microbiota is different levels of serum metabolites (Hsiao et al; 2013). This is because the offspring of the MIA model had symptoms of autism including deficiencies in pre-pulse inhibition, deficiencies in communication and repetitive behavior but also had elevated levels of certain serum metabolites (Hsiao et al; 2013). There were a plethora of different levels of serum metabolites between the autistic mice and normal mice (Hsiao et al; 2013). The metabolites believed to be most important in the cause of these Autism Spectrum Disorder symptoms were 4-ethylphenylsulfate and indolepyruvate (Hsiao et al; 2013). Both of these had significantly increased levels in MIA offspring such as 4-ethylphenylsulfate, which had a 46-fold increase (Hsiao et al; 2013). When naïve mice were given these metabolites independently they expressed elevated or reduced amounts of certain behavior (Hsiao et al; 2013). For example, 4-ethylphenylsulfate caused mice to express increased anxiety-like behavior (Hsiao et al; 2013). However, some behaviors were not present when 4-ethylphenylsulfate or indolepyruvate were given suggesting that these metabolites in combination with others cause ASD behavioral symptoms as well (Hsiao et al; 2013). When the MIA offspring were given Bacteroides fragilis in probiotic therapy, metabolite levels were reduced to normal including 4-ethylphenylsulfate and indolepyruvate (Hsiao et al; 2013). These same mice also showed that behavioral problems were ameliorated including communicative behavior, repetitive behavior and anxiety-like behavior after probiotic therapy (Hsiao et al; 2013). Intestinal barrier permeability integrity also increased meaning that fewer metabolites were leaked into the blood stream (Hsiao et al; 2013). This suggests that behavioral symptoms of the MIA model may be caused by extra metabolites leaking into the blood stream and circulating to other parts of the body (Hsiao et al; 2013).

The prevalence of autism in children exceeds juvenile diabetes, childhood cancer and pediatric AIDS combined (Kang et al; 2013). Scarily, there is still a rapidly growing rate of autism in the U.S. with 1 out of 88 children with autism as of 2008 (Hsiao et al; 2013). Fortunately, at the same time, there are new ideas that are rapidly emerging as well, including the gut-brain axis. This could serve as the foundation for many potential cures such as probiotic therapy for autism and neurological illnesses in general. We also know that elevated serum metabolite levels and decreased gut diversity may be the causes of autism. The altered immune system profile, specifically cytokines, in ASD provides insight into possible future immunological treatments such as blocking the production of certain cytokines. While the microbiota, gastrointestinal symptoms, ASD, the immune system and cytokines seem outlandish to link together and a discombobulated list, research proves otherwise. For example, research with GF mice showing the link of the absence of microbiota and associated alterations in the immune system to abnormal behavior supports the connection (Hsiao et al; 2012). On the other hand, we do not know exactly how these ideas, although shown, work. There are many questions to be posed on this upcoming topic such as how these starkly different ideas may be connected. Personally, I wonder how the lack of microbiota diversity could be the cause of the immunological abnormalities in children with ASD. In turn, how do these immunological abnormalities influence the brain and behavior? Cytokines? Additionally, could the blockage of cytokines and or the correction of their abnormal production be used to treat ASD? Finally, because of the rising prevalence of autism, I wonder about the role of new technologies and culture, such as the increased use of antibiotics, increased use of gut altering substances and a westernized diet on ASD?

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The Effect of Oil Spills and Natural Disasters on Marine Wildlife, by Isabella Brizzi (Sophomore)

Natural disasters can occur without warning and are often times detrimental to the environment as well as the species living within that specific habitat. Different natural disasters affect different species in various ways, both long term and short term. Some species may be drastically affected, resulting in death within the population. In consequence, such disasters may cause a significant decrease in a species population (Than, 2013). Exposure to deadly toxins or chemicals can weaken an organism's immune system and make that organism more susceptible to various diseases (Barron, 2012). An example of this would be the increase of deaths in the Dolphin species following Hurricane Sandy. Many of the dolphins who washed up on beaches after Hurricane Sandy were seen to have died of the Dolphin Morbillivirus, a virus belonging to the measles family (Watson, 2013). Over the span of the last couple of years, several natural disasters have occurred, including the Deepwater Horizon oil spill, Hurricane Katrina, and Hurricane Sandy.

The Deepwater Horizon Oil spill occurred off at sea in the gulf of Mexico, but still affected many plant and animal species along the coast of the Gulf. Over five million barrels of oil leaked into the sea. About 310 miles of the sea's floors and coasts along the Gulf were affected by this disaster with various levels of pollution. Chemical dispersants, such as Corexit 9500, were used to help clean up the oil after the Deepwater Horizon Oil Spill. Although these chemical dispersants helped, there were some negative effects as well (Gringley, 2013). According to Gringley, the chemical dispersants may have been one of the major causes to the illness of the majority of the aquatic species (Gringley, 2013). Although the chemical dispersants helped with a portion of the clean up, they did not eliminate the whole problem, because a large percentage of the oil from the Deepwater Horizon Oil spill still lays at the bottom of the ocean to this day (Pappas, 2014). This oil is re-washing up on shores, and is still affecting various species along the coast of the Gulf, in a continuous manner, leading to various levels of toxicity. Since the oil is still present, the habitats and various ecosystems within the Gulf and surrounding areas have not had a chance to completely recover from the disaster. The effects of both the oil and the chemical dispersants are variable, depending on the specific disaster as well as the amount of exposure the species receives. As seen with the Deepwater Horizon Oil Spill, numerous organisms, including both aquatic and other wildlife species, were found to have immunotoxic effects (Barron, 2012).

Like the Deepwater Horizon, although a different type of disaster, Hurricane Sandy, has caused just as much, if not more destruction to the environment on a large scale. Hurricane Sandy happened in 2012 and affected the eastern coast of the United States, causing unusual water patterns in the Atlantic Ocean. Much of these unusual water patterns were due to the mixing of different bodies of water, which changed the properties of the water. An example of this change is the temperature of the water.

After Hurricane Sandy the water temperatures seemed to have risen bringing in species that would have not normally have lived in that particular ecosystem (Bhattarai, 2014).

Dr. Saleh at NJIT, performed a study testing the coastal shores of the east coast, specifically, New Jersey, to test for changes in the water after Hurricane Sandy. Hurricane Sandy was observed to bring an increase of "brackish" waters to the eastern coast (Saleh, 2013). To test the extent of the damage on the coastal shores of New Jersey, three different ecosystems were studied. The three different ecosystems consisted of "sand beaches, wetlands and estuary residential areas" (Saleh, 2013). Within these studied locations, measurements of pore water, the water found between sentiment particles, was taken and then analyzed. Each was analyzed for the salinity in the water, the nutrients and the metals. The introductory results show that there was seem to be an increase of metals by three times as much as there was before Hurricane Sandy and the increased salinity did not return to normal for another two months (Saleh, 2013)

Throughout history, the pattern seems to continue ; natural disasters have a large effect on the environment and the species who inhabit these regions. Both Hurricane Sandy and the Deepwater Horizon oil spill happened several years ago, but still the affected areas and organisms have yet to fully recover to the way they were before the disaster. In the future, I firmly believe more studies should be conducted to learn about long term impacts that natural disasters like Sandy and the Deepwater Horizon Oil Spill, bring about. It would also be important in the future to conduct studies, in order to learn about the best dispersant to use in these scenarios, that would be the least harmful to the environment. Equally important, is the idea that strategies, should be created to be put into place immediately after a natural disaster occurs. These strategies would be useful because they would be able to help prevent some of the long term problems that can occur, for example if oil is released into the ocean again and stays there for a long period of time. In the future I would like to help with the discovery of these new dispersants and strategies in order to prevent the environment from further damage.

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Using Transparent Luminescent Solar Concentrators and Dye-Sensitized Solar Cells for Solar Energy, by Melanie Porras (Sophomore).

Solar energy can simply be regarded as the energy that comes from the sun ("Energy: The Solar Prospect," 2004). Solar panels take solar energy and convert it to electricity with the help of photovoltaic (PV) cells ("Energy: The Solar Prospect," 2004). Photovoltaic relates to the production of electrical current at the junction of two substances exposed to light (Marsden, 2001). Thus these photovoltaic cells create an electric field to produce electricity from solar energy (Marsden, 2001). To create this electric field, photovoltaic cells are composed of two silicon (semiconducting material) layers, one infused with phosphorus, making it a negative charge layer, and the other infused with boron, giving it a positive charge layer (Marsden, 2001). Like a magnetic field, which occurs due to opposite poles, an electric field occurs when opposite charges are separated (Marsden, 2001). After an electrical field is established, metal conductive plates are placed on the sides of the PV cell to collect the electrons and transfer them to wires (Marsden, 2001). These conductive plates are usually composed of electrodes, a conductor, through which electricity enters or leaves an object (Marsden, A. T. 2001). The PV cells then take the sun's photons, particles of light, to knock electrons free from the atoms of the semiconducting material, thus generating a flow of electricity. Several PV cells when put together are then able to create a solar panel or solar concentrator ("Energy: The Solar Prospect," 2004).

These PV cells are then able to produce solar con-

centrators, and in particular, transparent luminescent solar concentrators (Zhao, 2014). Solar concentrator means that it concentrates on light and converts it to heat, exactly what a solar panel does (Marsden, 2001). However these transparent luminescent solar concentrators (TLSCs) in particular are highly transparent in the visible spectrum (Zhao, 2014). What makes these TLSCs transparent is that they are not limited by chromophore, an atom whose presence is responsible for the color of a compound, absorption and emission in the visible spectrum which leads to a large degree of colored tinting (Zhao, 2014). To not be limited by chromophore absorption and emission the TLSCs have to absorb and emit near-infrared radiation (NIR) (Zhao, 2014). To produce near- infrared (NIR), TLSCs selectively harvest NIR photons by waveguiding deeper-NIR luminophore, an atom or atomic grouping in a chemical compound that displays luminescence, emission to high efficiency segmented solar cells (Zhao, 2014). These NIR emitting TLSCs are exactly what Yimu Zhao, a graduate student from Michigan State University, is working on (Zhao, 2014).

At Michigan State University, Yimu Zhao focuses on the development of luminophores blending with cyanine and cyanine salts, specifically CY and HITCI (Zhao, 2014). Zhao engineered certain molecules that can capture light and combined them with CY and HITCI, then integrated them into LSCs and saw its overall function (Zhao, 2014). The special LSCs were made by following a number of steps: first the organic salt solutions were prepared by dissolving CY and HITCI into dichloromethane solutions, each solutions transparency was then measured with a spectrometer, the emission spectra and quantum yield of various dyes were measured (Zhao, 2014). The glass was fabricated by mixing the dichloromethane solutions with a coating and placing them on glass. It dried for 2 hours and the process was repeated 3 times. Then a 7 cm × 0.1 cm PV cell was placed on the edge, when measurements were finally taken of the electrical output and efficiency (Zhao, 2014).

One of the results showed that when the CY and HITCI were in the form of concentrations, HITCI has a greater absorption percentage than CY, but CY had a greater quantum yield than HITCI. The quantum yield is a radiation-induced process where the number of times a specific event occurs per photon absorbed by the system (Zhao, 2014). In terms of absorption and emission spectra of the NIR-absorbing luminophores CY and HITCI films, both CY and HITCI had little visible absorption (Zhao, 2014). While CY had a stokes shift (wavelength difference between the absorption and emission peaks) of 30 nm, HITCI had a Stokes shift of 20 nm (Zhao, 2014). This gives CY a bigger advantage over HITCI because the bigger the Stokes shift the greater the quantum yield, and in essence a greater absorption (Zhao, 2014). However the Stoke shift can not get too big because then visible light will be absorbed rather than NIR (Zhao, 2014). Seeing that CY was essentially better than HITCI, Zhao decided to proceed to further experiment with only CY (Zhao, 2014).

Zhao concluded that overall TLSCs exhibit a non-tinted transparency of 86% in the visible spectrum combined with an efficiency of 0.4% and have the potential for efficiencies up to 10% (Zhao, 2014). It was then noted that the only difference between CY and HITCI was that CY had an extra side chain than HITCI (Zhao, 2014). So by increasing the number and/or polarity of these side chains, as well as central methine substitution, it may be possible to engineer visibly-transparent NIR luminophores with larger Stokes shift (Zhao, 2014). Unfortunately for an LSC to have an EQE, an overall absorption ratio, of about 4% the length of each LSC would have to be 0.04 meter; as the EQE increases the length of the LSC decreases. These transparent NIR LSCs provide a new route to transparent light-harvesting systems and have a tremendous potential for high defect tolerances and processability (Zhao, 2014).

On the other hand there are Gratzel cells, Dye-Sensitized Solar Cells (DSSCs), which also offer a path to cost-effective solar power (Klinger, Patel, Postma, 2012). The Dye-Sensitized Solar Cells do not require rare source materials nor high-grade semiconductor processing equipment, thus they are easy to fabricate. By losing some efficiency, a greater reduction in cost can be offered and simultaneously, the total price per kWh can also be reduced (Klinger, Patel, Postma, 2012). These carbon nanotubes offer a potentially cheaper and easier alternative to these materials, since they are not only photoactive, but they are also highly conductive, strong, and chemically inert (Klinger, Patel, Postma, 2012).

Both TLSCs and DSSCs offer new improvements in the field of solar energy. DSSCs offer an improvement in solar cells by increasing the efficiency while lowering the overall cost (Klinger, Patel, Postma, 2012). Transparent NIR LSCs can eliminate visual impact and minimize amount of expensive solar materials required while extending the photon harvesting range into the NIR (Zhao, 2014).

Not only are these improvements for solar energy but also for us at humans. TLSCs can one day offer us the ability to power buildings through windows, power a car through a windshield, or even help power a cell phone. The new advancements offer us a new and cleaner way to use energy in an eco-friendly way. And since solar energy is renewable we will never have to worry about there not being enough or running out anytime soon.

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Genetics of Bipolar Disorder and Schizophrenia, by Matthew Gofman (Sophomore)

Bipolar Disorder is a mental disorder causing phases of heightened mood and depression. The heightened mood is identified as either hypomania or mania, contingent on the occurrence of psychosis and how severe it is. Mania leads to one feeling uncharacteristically joyful, active, or ill-tempered. During this period, one tends to perform rash actions without considering the outcomes, and causes one to feel as if they do not need to sleep as much . This leads to phases of depression which causes breakdowns, lack of communicating through the eyes, and a pessimistic attitude (Anderson, Haddad, & Scott, 2012). Bipolar disease can be characterized in multiple ways. Bipolar I Disorder means that the patient has has one or more manic phase, while Bipolar II disorder means that the patient has had one or more hypomanic phase along with a phase characterized by extreme depression. People with milder symptoms may have cyclothymic disorder. If Bipolar Disorder arises as a result of narcotics or other medical issues, a distinct classification is given (American Psychiatric Association, 2013). The suicide rate for those with the disorder over twenty years of age is around six percent, and thirty to forty percent of those with bipolar disorder cause self-harm upon themselves in some form. Bipolar disorder puts people at greater risk of developing other mental illnesses such as drug abuse and anxiety disorder (Anderson, Haddad, & Scott, 2012). While it is not fully agreed upon the cause of Bipolar Disorder, environmental and genetic influences play a part in the possibility of developing the disease (Goodwin, 2012). The external factors that may play a role are chronic stress and a legacy of child maltreatment. In attempt to treat the disorder, patients are given psychotherapy and prescriptions such as antipsychotics and mood stabilizers, such as anticonvulsants and lithium. Electroconvulsive therapy is employed when other treatment does not work (Anderson, Haddad, & Scott, 2012). Bipolar disorder results in social, monetary and numerous other problems. These problems occur in up to 1/3 of those with Bipolar Disorder, with the threat of dying due to cardiovascular illnesses two times greater than for the average person. This is caused by the side effects of the narcotics given for treatment, along with bad decisions. Bipolar Disorder affects around 3% of those in America, the majority of people first experiencing indications of the disease at 25 years of age (Anderson, Haddad, & Scott, 2012). The rates for Bipolar Disorder are comparable in men and women (Diflorio, 2010). Along with this, Bipolar Disorder has a large effect of the economy, costing around $45 billion to the American government in years past (Hirschfeld, & Vornik, 2005). Bipolar Disorder is an illness that plagues many people, yet more information is being gathered about this disorder and how it is connected to numerous others. It has been hypothesizes that Bipolar Disorder and Schizophrenia are part of a larger umbrella disorder with many variations, from the milder form, cyclothymic D, to the more debilitating schizophrenia (Mahon, Eldridge, & Crocker, 2012).

Schizophrenia is a mental disorder causing uncharacteristic social conduct along with lacking the ability to identify reality. The symptoms of Schizophrenia are delusion, thought disorder, hallucination of sounds, decreased social activity, avolition, and lessened expression of emotions. Schizophrenia is diagnosed through witnessed actions and described occurrences. Due to the many symptom groupings, a disagreement exists within the medical field about whether Schizophrenia embodies a sole disorder or numerous distinct ones (Picchioni, & Murray, 2007). In spite of the communal perception that Schizophrenia suggests a split personality, Schizophrenia in fact infers a "splitting of mental functions" (Baucum, 2006). The core management of this disorder is antipsychotic treatment, which mainly subdues dopamine receptor action. Therapy, job guidance and societal restoration are similarly significant in dealing and managing Schizophrenia. When the patient becomes a danger to themselves or the people around them, hospitalization can become essential, yet due to recent improvements in treatment and care, visits to hospitals among Schizophrenia patients are quicker and less numerous (Becker, & Kilian, 2006). Indicators of Schizophrenia usually arise as young adults, and affects around 0.3–0.7% of individuals during their lives (Os, & Kapur, 2009). While Schizophrenia is usually associated with its affecting one's capability to reason,

it also leads to lingering difficulties with conduct and emotions. People with Schizophrenia are likely to have further disorders, such as those concerning anxiety and depression, and around half of those with Schizophrenia have had disorders regarding substance abuse in their lives (Buckley, Miller, Lehrer, & Castle, 2009). Additional complications such as joblessness, vagrancy, and poverty are prominent among those with Schizophrenia, and affected individuals also have a typical life expectancy of around 10-25 years shorter than the standard (Laursen, Munk-Olsen, & Vestergaard, 2012). This lower life expectancy is the outcome of amplified problems concerning well being such as a suicide rate of around 5 percent (Hor, & Taylor, 2010). One's surroundings, genetics, and psychological development all play a role in developing this disease, with certain narcotics seeming to begin or exacerbate symptoms (Picchioni, & Murray, 2007).

Numerous analyses on those with Bipolar Disorder and their kin have indicated that the illness is genetic, and can be passed down from family members. Possibly the most persuasive research comes from studies of identical twins. In these analyses, researches prove that if one of the twins has the illness, the other one is at a higher probability of also establishing the disorder than other relatives are. Scientists resolved that bipolar disorder is likely to evolve in up to 70% of twins, whose identical twin has the illness (American Psychiatric Association, 2013). This provides value implications on the genetic factors being Bipolar Disorder susceptibility. An analysis at John Hopkins University attempted to prove that Bipolar Disorder ran within the bloodline first-degree relatives. They concluded that kinsman of those with Bipolar II, also had Bipolar II 40% of the times, and that kinsman of those with Bipolar I, also had Bipolar II 22% of the times (American Psychiatric Association, 2013). The genetics behind this disorder have been researched profusely in order to determine why this is, such as a group of german researchers who analyzed heredity statistics from thousands of patients with and without Bipolar Disorders. In the most massive examination of the genetic grounds of Bipolar Disorder thus far, researchers compared the genetic makeup of close to 1,000 people with Bipolar Disorder with close to 15,000 without it (Muhleisen, Leber, & Schulze, 2014). Using their statistics, the researchers studied over two million unique genetic areas, in both study groups. Consequent assessments of these regions exposed five risk areas on deoxyribonucleic acid that are linked to the disorder. Of these areas, three of them, TRANK1, ODZ4, and ANK3, have previously been defined in past analyses, though have never been as statistically proven as in this study (Muhleisen, Leber, & Schulze, 2014). However, two of the areas of risk were exposed for the first time, MIR2113-POU3F2 on the sixth chromosome, and ADCY2 on the fifth chromosome. The scientist expressed notice to the ADCY2 region, as it cyphers an enzyme which has a large role in transferring messages to the nerve cells. This furthers the proven concept that the message transmission in specific areas of the brain is diminished in those with Bipolar Disorder. The findings of these areas of risk, predominantly the ADCY2 region, offer new understanding of the genetics behind Bipolar Disorder (Muhleisen, Leber, & Schulze, 2014). In another large research on Bipolar Disorder, researchers conducted an experiment to determine if the PCDHa protocadherin gene family is linked in bipolar disorder and Schizophrenia. They hypothesized that the 5q31-linked protocadherin family locus should be considered as potential candidate locus in schizophrenia and bipolar disorder family (Pedrosa, Stefanescu, & Petruolo, 2008). The results of the experiment proved this to be true, as in case of SNP rs31745, a significant increase in homozygosity for the minor allele (T) was detected in patients with bipolar disorder. The linkage studies suggest that the 5q31-linked PCDH locus should be more thoroughly considered as a disease-susceptibility locus in psychiatric disorders such as Bipolar Disorder and Schizophrenia, with rs31745 is a candidate allelic variant.This information can be used to understand susceptibility to Bipolar Disorder, and can allow doctors to predict who will get these diseases early on and potentially give them preventative medicine (Pedrosa, Stefanescu, & Petruolo, 2008). Such genetic research can also lead to further understanding of other mental illnesses such as Schizophrenia, in which similarities exist between certain subsets of the illnesses variants. Other studies have confirmed the possibility of Bipolar Disorder and Schizophrenia being part of an umbrella of various mental illnesses, albeit each one on extreme ends (Mahon, Eldridge, & Crocker, 2012).

The largest examination of schizophrenia has established 128 genetic variants connected with the disorder, found in 108 unique positions in the human genome. Around 37,000 patients with the disorder were compared with 113,000 people who do not have Schizophrenia (Makin, 2014). The study consisted of taking note of frequent mutations in the DNA in both groups of people. Genetic variations that occur frequently in those with the disorder are claimed to be connected with it, proving that that genetics do play a role is this disorder. While this study cannot classify the precise variants or genes that lead to this disorder, it points out parts of the genome that play a role in the possibility of developing Schizophrenia, also having implications for Bipolar Disorder susceptibility (Makin, 2014).

Bipolar Disorder and Schizophrenia are two disorders that affect 61.5 million Americans every year (Duckworth, 2013). New research is opening doors to our understanding of this umbrella of mental illnesses. In my future research, I hope to study precisely how and why these two disorders are connected, and to determine in what ways they are genetic. To be able to determine the genetic factors behind these two disorders would allow doctors to predict who will get these diseases and potentially give them preventative medicine. More than this, as more research is done in order to understand bipolar disorder and schizophrenia, the closer we are to a world in which they are not as prevalent, as the research can potentially allow scientists to create cures for these devastating mental illnesses..

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The Benefits of Music Therapy, by Kathryn Kenny (Sophomore)

What is music therapy? According to the American Music Therapy Association, Inc., "music therapy is the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program" (2014). Music therapy was first used during World War I in Veterans hospitals. It was used to help soldiers who were suffering from shell shock. In 1944 the worlds first music therapy program was established at Michigan State University. Today, more than seventy colleges have degree programs approved by the American Music Therapy Association. Just like many other therapies, music therapy has not been proven to completely heal a patient of any diseases. However, music therapy is an efficient treatment because it has the ability to enhance the quality of life for a subject. This certain type of therapy has the capability to promote healing, encourage emotional expression, relieve symptoms, and provide an overall sense of well-being ("Music Therapy", 2015).

Its been proven that both hemispheres of the brain process music. Music therapy has been shown to stimulate cognitive function and build other necessary functions. It has also been known to trigger communication, mood, social skills, and behavioral outcomes from patients. While listening to music, motor actions, emotions, and creativity are stimulated. Listening to a favorite song has the ability to connect the auditory brain areas and the hippocampus, a region in the brain, which is accountable for memory and social emotion consolidation. Music therapy can assist people who have physical, psychological, emotional, social, behavioral, cognitive, communicative, and or spiritual requirements or challenges. The parts of the brain that are associated with memory, attention, planning, and movement are shown to be stimulated while subjects are listening to music.

In the long run, listening to music greatly affects the superior temporal gyrus, which is located in the brain. It contributes in predicting whether someone likes a song or not. Throughout your life, the different genres one listens to will affect the way in which their superior temporal gyrus is formed. The more of a specific genre one listens to, the more they will cherish music of that genre (Landau, 2013). When reasoning with auditory music therapy, you have to consider a patients music interest. A study was done with 14 unpleasant, rebellious teenagers to see if listening to their prefered genre of music, which was rap, would improve their behavior in the foster homes in which they were living. They listened to music of their preferred genre throughout the week and one day each week there would be a meeting where the children would discuss the music and how it made them feel. Only rap music with positive lyrics was distributed among the children. The conclusion of the study showed that the participants were interested in the music. They each picked a certain line from a rap song that they liked best. Their behavior did tend to become better over the time of the experiment. This goes to show the effect of the genre of music used in music therapy (Tyson, 2002).

Music therapy is often used with elderly people. Music thanatology is a form of music therapy that is used at the end of a patients life to ease and soothe the death of a patient. Several studies have been conducted pertaining to the idea that music therapy can help victims with dementia gain memory. Dan Cohen was one who conducted this type of experiment. He explains in his documentary Alive Inside that music connects people with memories. Personal music does not count as medical intervention so doctors are unable to prescribe it to a patient. Doctors have yet to do anything

to touch the heart of a patient, medically speaking. Cohen describes that nursing homes and medication kills a victims spirit. What elderly people need is engagement. Music therapy gives subjects with dementia and alzheimers the opportunity to enhance the quality of their life and, in many cases, bring life back into them. Throughout the film, patients would immediately start to dance and recollect memories from their teenage years right after their chosen music started playing. As you can tell patients with dementia are just some of many that benefit greatly to music therapy (Rossato-Bennett, 2014).

Music therapy comes in several different variations. The most popular form of music therapy is auditory. Despite this, music therapy also comes in through forms of playing instruments and creating original music. A study was done in Los Angeles where children with limited opportunities, due to low income, ages ranging from 7-9, were given music lessons twice a week for a year. These children were bilingual and constantly did poorly on their standardized tests. The hypothesis of the experiment was that the scientists thought, by the end of the year, the children with the musical experience would perform better on standardized tests than the control group of children. The argument was that scientists running this experiment believed music training enhances language and reading skills. The study showed that after one year of musical training, the experimental group maintained their ages normal performance on the standardized while the control group's scores declined greatly. It was inferred, by the results of the experiment, that musical training is a way to keep a child's literacy development on track (Slater, Strait, Skoe, O'Connell, Thompson, Kraus, 2014).

Another study was done with 60 healthy females, where scientists were able to see the relationship between music therapy, stress and anxiety. These women, ages averaged at 25, were given a standardized psychosocial laboratory procedure and questionnaires to determine their stress and anxiety levels as well as their heart rate. The subjects were put in a comfortable chair with headphones and their choice of preferred genre of music. Although pop was the most popular genre chosen, classical was also very prominent in the chosen genre. The results of the experiment showed that stress and anxiety levels changed overtime. Cardiac measures also changed over the time of the experiment. Music has been shown to affect cognitive, emotional, and physiological processes for the better. Listening to music does positive things, like decrease sympathetic activity and trigger positive emotions. This experiment shows us that music can be beneficially to stress and anxiety (Thoma, La Marca, Brönnimann, Finkel, Ehlert, Nater, 2013).

As you can see, music therapy is a rising remedy that could potentially be used to treat patients with different diseases all over the world. Although there are pills and different medicines that are used to help cure and handle illnesses, these medications do not have the ability to touch the heart and improve the life of patients. Music therapy allows sick people to create, play, or listen to music that they enjoy. This could be extremely beneficial to our society today because we have lost the ability to make patients happy, especially in places like nursing homes. This is why giving music to patients with dementia and alzheimers is so important. It brings out the life and memories in everyone, and should be seriously considered for treatment of all different diseases in the near future.

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Vitiligo: An Autoimmune Disease, by Mistry Deepa (Sophomore)

Vitiligo is an autoimmune disease where the immune system attacks normal skin cells in the body, creating white patches on the skin (Rashighi et al., 2014). The skin cells that are destroyed are called melanocytes which contain pigment and reside in the epidermis between hair follicles (Nordqvist, 2014). A chemical called melanin is responsible for pigment, protecting the skin from sun burns, damage, and imparts the skin to its normal skin color (Rashighi et al., 2014). When the melanocytes are destroyed, the epidermis in the affected areas loses its normal skin color, turns white, and becomes susceptible to sunburn (Nordqvist, 2014). For unknown reasons, hair follicles and hair is usually spared in the areas of lesional skin, but it is observed and reported to be a sign of repigmentation, when skin around the hair follicle has pigment showing a freckle-like appearance (Nordqvist, 2014).

Typically vitiligo is diagnosed in young patients, 25% of them being of age 10 or younger and 50% being the age of 20 and younger (Stoppler, 2014). Affecting only less than 2% of the population, vitiligo usually begins spreading around the eyes, mouth, lips, fingers, wrist and feet but can spread anywhere (Stoppler, 2014). In most cases, depigmentation spreads slowly, over the course of several years (Stoppler, 2014). Vitiligo does not directly impact certain ethnic groups more than others, it is simply the fact that it can be seen on people with darker skin tones(Stoppler, 2014).

There are two types of vitiligo, segmental and non-segmental (Nordqvist, 2014). Segmental vitiligo

occurs in 10% of vitiligo patients, spreading rapidly and dramatically, affecting about 30% of children with vitiligo (Nordqvist, 2014). Non-Segmental vitiligo occurs in 90% of vitiligo patients and is more stable with a symmetrical pattern and lesional skin usually appearing on the face, neck, hands, elbows, feet, knees, fingers, arms, eyes, and mouth (Nordqvist, 2014).

In order to repigment, the epidermis needs to produce new melanocytes which can be found in a reservoir within the hair follicle (Nordqvist, 2014). These melanocytes can spread and migrate out of the hair follicles to the surrounding skin with therapies producing freckle-like appearances (Nordqvist, 2014). This is one of the reasons why smooth skin called glabrous skin does not have the ability to repigment with current therapies because of the lack of hair (Nordqvist, 2014). This skin can be found on the ventral surface of the wrists, on fingers, palms, feet, and lips (Nordqvist, 2014). The eyelids however seem to disregard this pattern as they tend to respond very well with repigmentation therapies (Nordqvist, 2014).

There are available treatments for vitiligo but many do not provide repigmentation for all patients (Nordqvist, 2014). Topical corticosteroids are steroid creams used to allow for repigmentation but is very unreliable and has many side effects (Stoppler, 2014). Similarly the treatment of phototherapy with UVB light and phototherapy with UVA light is also unreliable and unpredictable (Stoppler, 2014). Another method of repigmentation is skin grafting but it is not recommended in children and can cause scarring in two places of the body, the site of the skin graft and the area on the body where the skin is removed for the graft (Nordqvist, 2014).

Previous studies show that melanocytes are killed by cytotoxic T-cells consequently destroying the pigment and causing the white spots to form on the skin (Rashighi et al., 2014). Specifically, the CD8+T cells have been found to cause the lesional skin and is also found in large quantities in these areas (Rashighi et al., 2014). These cells are found to be signaled by the CXCL10 IFN-gamma protein (Rashighi et al., 2014).

A nude mouse model was created to replicate human vitiligo (Harris et al. 2012). The model is hairless, has no thymus and therefore is unable to produce T cells (Harris et al. 2012). This allows for the mouse to accept tumors or transplants from humans or other animals (Harris et al. 2012). The mouse model replicated human vitiligo exactly and studies have proven that the neutralization of the protein CXCL10 with CXCL10-/- allows for repigmentation (Rashighi et al., 2014). CXCL10 is found to be a cause for the depigmentation in vitiligo but the underlying cause as to why there is an overproduction of this protein is unknown (Rashighi et al., 2014).

As vitiligo has been noted to be an autoimmune disease, many scientists also believe that it has other underlying causes. A study proves that oxidative stress was a key factor in egyptian vitiligo patients (Mehaney et al., 2014). Similarly, serum 25-hydroxyvitamin D deficiency was also noted to be a prime element in chinese vitiligo patients (Xu, Fu, & Wu, 2012). A protein called HSP70i is known to play a vital role in autoimmune diseases such as vitiligo (Loyola University Health System, 2013). When a study was done to correct the mutation in this protein on mouse models, the depigmentation fur on the mice was corrected and the fur was it's normal color once again (Loyola University Health System, 2013).

Patients on vitiligo forums have said that they have had the onset of vitiligo after becoming sick with a cold or fever. The sickness of the systemic symptoms could have triggered the gene that causes vitiligo to express itself or the virus infecting the body itself could have altered the gene for vitiligo. This gene change would cause increased chances of the onset of vitiligo with increased levels of oxidative stress, vitamin D deficiency, weakened immune system, and family history. The emergence of vitiligo could be associated with a combination of these factors and more.

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The Vulnerability Connection between Bullying and Cults and Terrorism, by Jackson Heichel (Sophomore)

Humans. We're a sorry bunch, aren't we? We always seem to find something to fight about, be it religion, about rights, about a million things that, in the end, barely matter. But somehow, at the same time, we always want to fit in. From when babies are just developing, they are imposed upon by their parents. Depending on how much affection kids are given, they can go in one of two ways. This is called Anxious Avoidance Attachment. It is actually marked by two distinct sections. The first, Anxious Attachment, which is when you want people to like you, comes about from children receiving a large amount of attention as a young child. This creates a response in which an adult has a desire to have a lot of positive reinforcement. Avoidance Attachment is when the opposite happens, when a person receives little attention as a child and as a result becomes more independent from others, sometimes becoming anti-social (Körner & Volk, 2014). In both cases, the human animal is one that wants to find somewhere where they feel more accepted.

Acceptance can be difficult to find, however. One of the most common problems facing the younger generation is that of bullying. In a study done by the Olweus Bullying Prevention Program, using the Olweus Bullying Questionnaire, which included 1000 girls and 1000 boys, it was found that the highest prevalence of bullying was in the third and fourth grades. In addition, 18% of all students were involved in bullying in some way. This may have meant that the student was a bully themselves, they may have been bullied, or both. The study also found that cyberbullying was one of the least common types of bullying. (Mullen, 2014). It seems apparent then, that a bullying victim may choose to go to the internet over a person they might know in real life. This is further exasperated by the statistic that states that, by high school, only 36% of students thought that a teacher or administrator would try to help a bullied student. (Mullen, 2014).

So, clearly, kids are going to the internet for a community when their own community fails them. This makes sense, as a study by Catalina Toma of the University of Wisconsin-Madison working with graduate student Mina Choi found that going on social media sites, such as Twitter, Facebook and Instagram can intensify emotions. Sharing bad news on a social media site makes the news more real and can make a person more depressed than they had been. Similarly, sharing good news makes a person happier, and more likely to share these feelings further (Choi & Toma 2014). These claims are further substantiated by reactions to the news that you share. People are more likely to respond to a positive stimuli from a friend or team member than a negative stimuli.(Cikara, Bruneau, Van Bavel, & Saxe, 2014). In this way, a complete stranger who just happens to be friends with you on Facebook might express their sorrow at your bad news faster than someone you might have seen earlier that day. This response triggers an emotional connection to this person, and this means that you are likely to become closer to one another,

So, why could this be bad for anyone? More friends are always a good thing, right? A larger support system leads to more support, one would assume. This is true, in most cases. Sometimes, however, the friends you make might not be the kind of friends you would like to have. One example might be a kid who does drugs or smokes. Due to the desire to be accepted, one might be more likely to smoke when around this friend. (Körner & Volk, 2014). Another example would be if one were to get involved with another person whose personality does not mesh well with their own, leading to fighting and emotional distress. The last example is one that seems a bit more extreme. Some misguided people, in their search to be accepted, may find themselves surrounded by terrorists online. Groups like Iraq and Syria Islamic State, or ISIS and the Taliban are now frequently using social media to connect with kids and try to convince them of their way of thinking. If a lonely tenager, who has lost faith in the teachers and administrators they used to look up to, and is searching for a place to belong was to find one of these people, they will be exploited. A person who has been bullied, and henceforth becomes a bully has certain characteristics that identify them as a bully-victim. These traits include being aggressive, or anxious. Sound familiar? That sounds like two traits one would use to describe a terrorist. (Felipe, Garcia, Babarro & Arias, 2011). In addition, terrorist groups that find a person who matches these traits will zero in on this person, find out exactly how to manipulate them, looking at past statuses that they have access to now, because the terrorist group is a friend on Facebook. The group would begin to wear them down, talking about the faith they have in their god, about their religion and how happy it makes them. With hearing the continued descriptions of how their friends faith completes them, anyone would become curious. Suddenly, they find a religion that may promise eternal life, and beautiful women who will love and cherish them. These basic tenets of human need are satisfied, and soon, the kid who only a few weeks ago was getting picked on is part of a powerful terrorist organization that wants to destroy the rest of the world. Then, when they are asked to continue in this faith, and must attack someone, or a place, the same forces that

drove a person to find this group will drive them to do whatever it takes to stay with them. (Körner & Volk, 2014).

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Possibilities of Treating Alzheimer's With Bispecific Antibodies, by Margaret Gruber (Freshman)

Dementia is defined as a loss of cognitive function that interferes with a person's executive functions or mental ability. (Alzheimer's Association, "Dementia," 2015). The type of dementia most people are familiar with is Alzheimer's disease, a neurodegenerative disease that breaks down synapses and worsens the memory of the patient until they pass away because of the brain tissue loss. These cause memory loss, decline in cognitive function, speech impediments and eventually death. The disease is characterized by beta-amyloid plaques and tau protein tangles, which cause the symptoms of Alzheimer's. (Alzheimer's Association, "Facts and Figures," 2015).

There are two types of Alzheimer's disease, early-onset and late-onset. Early-onset affects people who are around middle-aged and is usually genetic, while late-onset appears in people that are in their 60's or 70's. Once the symptoms become clear, Alzheimer's patients are expected to live for about eight more years. The disease mainly affects memory, but it also affects speech and general cognitive function. 500,000 people die from Alzheimer's each year, and a cure has yet to be found. (Alzheimer's Association,"What Is Alzheimer's," 2015).

Buildup of beta-amyloid, a protein found in the fat of nerve cells, is a debated cause of Alzheimer's. Scientists speculate that it possibly aids in cell attachment. (Genetics Home Reference, "APP," 2012). However, the function of beta-amyloid in Alzheimer's disease is clear. An enzyme called BACE-1 abnormally cleaves the beta-amyloid protein, which causes it to aggregate together and form the plaques. (Watts, "Boosting Brain Uptake of a Therapeutic Possibilities of Treating Alzheimer's Antibody by Reducing Its Affinity for a Transcytosis Target," 2011). Along with these plaques, small aggregates of the protein form that block synapse communication and possibly activate immune cells that cause inflammation and kill inactive cells. (Alzheimer's Association, "Plaques," 2015). Along with beta-amyloid, the tau protein debatedly causes Alzheimer's by forming neurofibrillary tangles in protein cellular transport systems. Tau normally stabilizes microtubules and keeps transport systems in order, but when they fail, tau begins to build up and form the neurofibrillary tangles that cause a blockage in the transport systems and destabilizes them. This blockage prevents nutrients and other essential materials for the brain from entering cells, which causes cell death. (Mandal, "What Are Tau Proteins," 2014).

While treatments have been developed and many clinical trials are underway concerning Alzheimer's disease, the blood-brain barrier prevents most treatment from reaching the brain in the first place. Formed by capillary endothelial cells, it is a barrier that protects the brain connected by tight junctions that only allow specific nutrients and substances into the brain. (Ballabh, "Structure of the Blood-Brain Barrier and Its Role in the Transport of Amino Acids," 2006). Because of how selective the BBB is, it is difficult to create an Alzheimer's treatment that is able to cross it. One material that can cross the BBB is transferrin, a protein that transports iron ions into the brain and other organs. It bonds to the ions in four places, sealing it in, until it can find a transferrin receptor on a cell. Once it attaches to the receptor, the transferrin can release the iron into the cell. Transferrin is one of the proteins able to transport materials across the BBB (specifically iron) and does so by latching onto receptors on the BBB. (Goodsell, "Ferritin and Transferrin," 2002).

However, an antibody treatment for Alzheimer's has been developed that can pass the BBB. It is a bispecific antibody, meaning that it has two arms that each have a different receptor. One arm of this antibody attaches to transferrin to let it cross the BBB, and the other inhibits the BACE-1 enzyme. By attaching to transferrin, it was able to cross the BBB with high distribution and crossing rates. Specifically, the antibody is anti-TfR (transferrin), meaning that it is not tightly attached to the

transferrin, making it easier to cross the BBB, as it can let go of the transferrin easily and enter the brain. A high-affinity antibody cannot transfer at as high a rate as a low-affinity antibody, because it remains attached to the transferrin with a much tighter bond. The BACE-1 inhibiting side of the antibody (which has a higher affinity) prevents the enzyme from cutting beta-amyloid abnormally, which lowered plaque creation greatly. However, this antibody does not treat tau protein tangles, so another solution must be found in order to treat both components of Alzheimer's efficiently. Even so, this anti-TfR antibody was highly successful, and can offer a successful treatment for Alzheimer's in the future. (Watts, "Boosting Brain Uptake of a Therapeutic Antibody by Reducing Its Affinity for a Transcytosis Target," 2011). The drawbacks to the antibody are slim, but may have a large impact upon humans. Reticulocytes, young red blood cells, were reduced by 10% in mice, along with symptoms of lethargy and muscle spasms caused by the antibody, but most symptoms, excluding the blood cell loss, disappeared after some hours. Young red blood cells are extremely important carriers of iron and hemoglobin, which ensures that oxygen can be delivered and iron as well. The cells use transferrin to deliver this iron, however, and an antibody that attaches to transferrin can possibly prevent red blood cells from accumulating iron, which in turn prevents other cells from getting iron. Removal of an Fc effector in the anti-TfR aspect of the antibody, however, prevented red blood cell loss. (Watts, "Addressing Safety Liabilities of TfR Bispecific Antibodies That Cross the Blood-Brain Barrier," 2013).

According to Fierce Biotech, the failure rate of Alzheimer's clinical trials is 99.6%. (Carroll, "Alzheimer's R&D suffers as trial failure rate hits an 'astounding' 99.6%," 2014). Considering the difficulty of crossing the BBB and how protected the brain itself is, this is not a surprising statistic. The anti-TfR antibody's ability to cross the BBB can possibly lower the chances of failure, but it cannot be proven until clinical trials actually ensue. Along with this challenge, the fact that the antibody does not treat tau is also an obstacle in the way of finding a successful treatment for Alzheimer's. The antibody is still a valuable foundation for a treatment, and more research can refine it and ensure it prevents both beta-amyloid plaques and tau neurofibrillary tangles.

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Developing Antimicrobial Polymers to Potentially Replace Conventional Antibiotics, by Theodora Worledge (Freshman)

At least 2 million people every year in the U.S. are infected with antibiotic-resistant bacteria, and at least 23,000 die as a direct result of the infection. Many others also die from separate medical conditions compounded with an antibiotic-resistant infection (U.S. Department of Health and Human Services [HHS], 2013). The continued rise of bacterial resistance is projected to kill 10 million people per year by 2050, overtaking cancer's projected death toll, cost the world 100 trillion USD, and reduce the Gross-Domestic Product by 2% to 3.5% (Review on Antimicrobial Resistance, 2014).

Since conventional antibiotics are facing increasing resistance from bacteria, it is vital to obtain a convenient and efficient antimicrobial agent. Conventional antibiotics simply insert into the bacterial or fungal membrane and target specific functions of the microbe, such as the syntheses of DNA, RNA, cell wall, and protein. Because microbe morphology is preserved, microbes develop resistance to these antibiotics (Brogden, 2005). Methicillin-resistant Staphylococcus aureus (MRSA), which is the leading cause of healthcare associated infections, and vancomycin-resistant Enterococci (VRE) are two examples of antibiotic-resistant bacteria (HHS, 2013).

Bacteria are classified as two types. Gram positive bacteria simply have a highly cross-linked peptidoglycan wall as the outermost layer, constituting a thin and easily penetrable membrane. Gram negative bacteria have an additional barrier containing lipopolysaccharide (LPS) in addition to a highly cross-linked peptidoglycan wall, resulting in a thick outer wall. In appropriate environments,

both types of bacteria can form biofilms, thick layers of bacteria that form on solid surfaces submerged in aqueous solutions. Because of the multiple layers of bacteria in a biofilm, it is difficult to completely eliminate the bacteria within the structure; bacteria in biofilms are 1000 times more tolerant to antibiotics than free-floating bacteria (Tenke, 2004). Biofilms often form on implants and other medical devices, posing a threat to patients in hospitals and especially to those who have recently received surgery.

The next generation of antimicrobial agents may potentially be antimicrobial peptides and polymers. Both antimicrobial peptides and polymers selectively target and lyse bacteria by attaching to the negative microbial membrane with hydrophilic components and rupturing the lipid domain of the membrane with hydrophobic components. The physical nature of this interaction destroys bacteria morphology and therefore eliminates microbial resistance (Yeaman, 2003; Kenawy, 2007).

Despite the positive outlook for antimicrobial peptides, they possess several drawbacks. Antimicrobial peptides are susceptible to enzymatic degradation, expensive to produce, and cytotoxic to the mammalian cells (Marr, 2006; Hancock, 2006). Also, none have yet received FDA approval for public use (Hancock, 2006).

As Palermo, E.F., Kuroda, K. report, antimicrobial polymers have been found to overcome these obstacles that limit antimicrobial peptides (as cited in). The lack of biocompatibility of these polymers have been a problem in vivo, but biodegradable and biocompatible amphiphilic triblock polycarbonates that self assemble to cationic spherical micelles have been developed as a successful solution. Unfortunately, while these polymers were effective against drug-resistant gram positive bacteria, they had no impact on any of the gram negative bacteria tested (Nederberg, 2011).

Gram negative bacteria has an additional membrane composed of lipopolysaccharides (LPS) and proteins, which is an additional barrier an agent must cross before penetrating the peptidoglycan membrane to destroy the cell. Interaction between the hydrophobic components and the LPS and peptidoglycan barriers is crucial for lysis. The lack of effectiveness against gram negative bacteria is because the self-assembled cationic micelles shield their hydrophobic components within the cationic components, limiting the interaction between the hydrophobic components and the multiple gram negative bacterial membranes (Qiao, 2011).

Random copolymers have been found to assemble dynamic micelles exposing both cationic and hydrophobic components. These dynamic micelles are capable of efficiently lysing both gram positive and negative bacteria while retaining the characteristic of higher selectivity for bacteria than mammalian cells (Qiao, 2011).

Due to the prevalent threat of bacteria emphasized by increasing microbial resistance to conventional antibiotics, it is vital for a new antimicrobial agent to be found. Antimicrobial polymers are an increasingly attractive option, considering their high selectivity for bacteria over that for mammalian cells, potency towards both gram negative and positive bacteria, and ability to avoid development of bacterial resistance. Unlike present antibiotics, antimicrobial polymers can potentially solve humanity's war against bacteria once and for all.

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A Possible Link Between Alzheimer's Disease and Traumatic Brain Injury, by Clio Lieberman (Junior)

Introduction

Alzheimer's disease affects 30 million people worldwide. It is an advance form of dementia, which includes an early onset (EOAD) and a late onset (LOAD) form. EOAD is thought to be genetic, while LOAD is thought to be caused by different proteins in the brain. The first hypothesis is the amyloid-beta hypothesis, caused by the beta cleaved 39-42 amino acid chain of the amyloid precursor protein. Another hypothesis is the tau protein hypothesis, which is caused by hyperphosphorylated 383-441 chain tau proteins in the AD adult brain. This leads to cognitive damage, memory loss, speech impairment, inability to perform basic motor functions, and synaptic loss.

Traumatic Brain Injury

Traumatic brain injuries can be characterized in three ways: "(i) 'primary' blast effects that are linked to overpressure (BOP) events; (ii) 'secondary' blast effects caused by fragmented objects or shrapnel that can inflict blunt or penetrating trauma when hitting the head; and (iii) 'tertiary' effects caused by acceleration/deceleration as the head is propelled through the air" (Huber et al., 2013). This can cause "disorientation, confusion, neuronal swelling, reactive gliosis, myelin disruption, loss of consciousness, subdural hematomas, cerebral hemorrhage, and edema" (Huber et al., 2013) in the brain. The primary internal sign of a TBI is "diffuse axonal injury (DAI), which consists of axonal shearing" (Abisambra and Scheff, 2014). This axonal shearing can trigger a tau pathology cascade, resulting in even further tissue damage.

Amyloid beta hypothesis AB

APP, the amyloid precursor protein, is a "type one membrane glycoprotein" (Nalivaeva et Turner, 2013). APP is used in the developing brain "for neuronal precursor cells to migrate correctly in the nascent cortical plate" (Nativaeva et Turner, 2013), regulates "synaptic vesicle exocytosis" (Nativaeva et Turner, 2013), and maintains the use of calcium in neurons, which is used in synaptic transmission.

According to the first hypothesis, amyloid-beta proteins cause AD via the 39-42 amino acid chain of the amyloid precursor protein. The AB39-42 is cleaved by BACE-1, which is composed of three proteases, b-secretase, a-secretase, and y-secretase. The different secretases cleave APP at different places on the peptide. When a-secretase cleaves APP, it can be absorbed into the cell. When b-secretase and y-secretase cleave APP, it cannot be absorbed into the cell, and the oligomers aggregate in the extracellular matrix. Aggregated amyloid-beta oligomers attack the cell, causing cell death.

When APP is not cleaved properly, cell death occurs. Cognitive decline is also caused by the accumulation of APP. This happens in two different ways: when there is an overproduction of aggregated AB39-42, or when neprilysin (NEP), the APP degrading peptidase, malfunctions/is down regulated. Amyloid beta proteins are toxic and insoluble, which makes it difficult to remove if NEP is not produced.

Amyloid beta proteins also cause malfunctions in the blood brain barrier (BBB), and disrupt cerebral blood flow (CBF). AB39-42 causes leakiness in the BBB, which can let toxic macromolecules into the brain. According to Abbott et al. (2010), "leakage of these large molecular weight serum proteins into [the] brain across a damaged BBB can have serious pathological consequences." When there are holes in the BBB, it can lead to toxic macromolecules, such as glutamate, going through the BBB and into the brain (Bamburg and Bloom 2009). This can disrupt normal neuronal functions, like tight junctions in the neurons, causing cognitive decline.

Tau hypothesis

Tau proteins in the brain have six isoforms, ranging from 383-441 amino acids in length in the human adult brain (AnaSpec 2013). Tau can self-assemble into filaments (Bamburg and Bloom, 2009), which comprise neurofibrillary tangles. When self assembled, they "detach from the microtubules, thereby destabilizing microtubules and compromising axonal transport" (Hampel et al., 2010). They are also comprised of microtubule binding sites, which "form[s] the core structure" (Bamburg and Bloom, 2009) of the tau protein. These aggregated fibers are hyperphosphorylated, with at least 30 phosphorylation sites (Bamburg and Bloom 2009), which can compromise microtubules. "[P]hosphorylation at those sites might represent a switch from an intracellular environment that is non-permissive for tau self-assembly to one that is permissive" (Bamburg and Bloom 2009). This means that when tau is phosphorylated, it becomes active, and that when tau fails to self-assemble in absence of phosphorylation, it does not affect the cell.

Tau affects mitochondria in cells. It completely changes the structures of mitochondria, which become, "shorter organelles that undergo enlargement, cristae disorganization, and complete loss of inner structures and… decrease of mitochondrial mass" (Amadoro et al.,). The abnormal mitochondria are then removed by lysosomes in affected cells (Amadoro et al., 2014). This leads to a reduction in the ATP produced in a cell, which slows down and impairs important cellular reactions. This leads to cell death and cognitive loss.

Tau and AB interactions

Tau and amyloid beta proteins are both possible causes of AD in the brain,

and many scientists believe that "AB-oligomers as well as…AB-extracts from human AD brain induce AD type of tau hyperphosphorylation in cultured neurons" (Bamburg and Bloom 2009). It has been shown that AB induces hyperphosphorylation in cells, leading to tau-induced cell death, releasing toxic tau-related proteins in the CSF (Hampel et al., 2010). This means that hyperphosphorylated tau in the AD brain may be caused by amyloid beta proteins in the cell. Amyloid beta proteins and tau may interact to damage mitochondria and cells as a whole. Affected mitochondria are described as "roundish and pale with patchy matrices, sometimes swollen and suffering from the total disappearance of their inner cristae" (Amadoro et al., 2014), and with "irregular and interrupted intermembrane space" (Amadoro et al., 2014). The destruction may result in cell death, since mitochondria would not be able to make enough ATP to perform normal life functions.

Glycogen synthase kinase 3 (GSK3) interacts with both tau and APP by modifying both of their substrates, promoting the phosphorylation of tau, and causing BACE-1 to use b-secretase to cleave APP. This promotes abnormal cleavage of AB39-42. GSK3 induces the hyperphosphorylation of tau, destabilizing microtubules in the brain, and leading to the cleaving of toxic AB, causing cell and mitochondrial death in neurons, with "intracellular components are released into the extracellular space" (Hernandez and Avila, 2008). This is toxic to the surrounding neurons, causing cognitive impairment, which not only affects the neuron affected specifically by AB, but the neurons surrounding it as well. GSK3 may also promote the overproduction of amyloid beta proteins, amplifying cell death in the AD brain.

Traumatic Brain Injury Interactions with Amyloid Beta and Tau Proteins

When a traumatic brain injury occurs, diffuse axonal injury (DAI) occurs in the affected tissue. DAI "distort[s] and break[s] microtubules" (Abisambra and Scheff, 2014), detaching tau and compromising the plasma membrane. This releases tau into the extracellular matrix before it aggregates. The tau then misfolds because of the "activation of tau-acting kinases and abrogation of protein phosphatase 2A activity, a tau phosphatase… result[ing] was enrichment of phospho-tau species"(Abisambra and Scheff, 2014). Tau then hyperphosphorylates, undergoes oligomerization, and finally aggregates, attacking cells (such as neurons and glial cells), and going into the CSF. This aggregated tau then "disturb[s] proteostasis and initiat[es] cytotoxic cascades" (Abisambra and Scheff, 2014), further leading to cellular damage.

TBI also increases production and impairs the clearance of AB39-42 in the brain after injury. TBI leads to an increase of extracellular glutamate through induced BBB leakiness, which increases intracellular calcium, which then increases mitochondrial oxidative stress, which leads to more disruption in the production of ATP. Oxidative stress then leads to caspase activation, leading to cell death, but also upregulating BACE1, which therein increases AB production. An increase of AB also leads to an increase in intracellular calcium, mitochondrial oxidative stress, and caspase activation, creating a cycle of increased cell death following TBI (Walker and Tesco, 2013). This increase in AB leads to a downstream increase in tau production and aggregation, leading to even more cognitive damage.

Conclusion

Amyloid beta proteins and phosphorylated tau are both abnormal forms of normal proteins found in non-AD brains. TBI is a major cause in the aggregation of amyloid-beta and tau proteins, leading to increased disruption in cellular activities, including synaptic transmission and ATP production. This leads to cell death, and an affect of this cell death is cognitive impairment, including memory loss, speech deficits, motor loss, dementia, and synaptic loss.

Mentor: Dr. Dara Dickstein, Ph.D.

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