

Personal Statement: I come from a place where life often makes it hard for people to leave—Ludlow, Mississippi. There are not many “success” stories, just people doing the best that they can with what they have and without what history and systemic disadvantage have denied them. There are opportunities but, as geographer Clyde Woods has written powerfully about, those opportunities are often arrested. In Ludlow, the idea that someone like me would, or even could, grow beyond these challenges and want to go to college, or want to be a scientist or medical doctor, is not so much an idea as it is a dream.

Yet, here I am, a dreamer. I left the place that people don’t leave (though I still carry the lessons and love of that place with me wherever I go). I am trying to write the story that people do not write, even if I’ve sometimes had to write it in unconventional ways. That has been my story—an unconventional journey from an unconventional place, all made possible by the audacity to dream and the good fortune of good people to help me make those dreams real.

College was never the first or second option, so throughout high school I took some detours including joining the Mississippi Army National Guard and attending vocational school becoming certified in carpentry to direct my career into the military and/or trade industry. During my junior year of high school, I received an opportunity to attend APEX, a leadership summit at the University of Mississippi. Attending this conference was my first encounter with a college campus and is the reason I chose to further my education. Not having a roadmap on how to get to college, I worked diligently with numerous individuals who were able to aid me in my admittance. From that moment, my journey of self-discovery began. My foremost goal was and is guided by dreaming big, but, becoming even bigger. My resilience and determination continuously move the finish line to define my own success.

As a senior in high school, I was determined to escape the society that I had called home for 17 years, but it was adamant to keep me. Battling one college application, one scholarship application, my peers, and even my family, I fell into a state that to this day cannot be medically explained. Almost five years later, I still have no recollection of any memories for ten days. Ten days that were spent in Brentwood Mental Health and Behavior Facility. Diagnosed as a severe and highly irreversible case of Psychosis, as a 17-year old high school student, I was faced with a task to become a healthy teenager again. Struggling with my speech, learning to walk in a normal fashion, but most of all having to teach myself how to write again was by far the most difficult and humbling time of my life that fostered a passion, a passion that helped me become a first generation college student and now pursuing a doctoral degree. A passion that still drives me today to study the brain.

During my undergraduate tenure, I sought opportunity and new learning environments every chance I saw. My general admission into Ole Miss was granted with the Luckyday Scholarship (essay and financial based award bestowed on 80 Mississippi residents showing leadership qualities and a strong academic background); Academic Excellence (an ACT scholarship award for those who score a cumulative 25); Bledsoe Scholarship (an academic award for those with a 3.0 cumulative GPA that must be maintained); Chancellor’s Leadership Scholarship (an award given to 75 students who showed strong leadership skills from across the U.S. that were nominated by faculty); and low-income federal and state financial assistance.

My initial awards did not stop me from seeking out other sources of funding for my education. Additionally, I received a Global Engagement scholarship, the Dr. Pepper SEC study abroad scholarship, an award from McDonnell Foundation to study Classics, and a Mildred Classics Scholarship Award to study Classics and Latin. As an undergrad., I was a member of numerous organizations and a participant of several honorable events including: UofM Pulse Leadership

Conference, Eta Sigma Phi Honor Society, the Society of Collegiate Leadership and Achievement, the National Society of Collegiate Scholars, a member of Phi Beta Sigma Fraternity Inc., Ole Miss Ambassadors, and even started an organization, Minority Association of Pre-Medical Students. Other accolades include receiving a Distinguished Research Citation from UofM School of Pharmacy, a feature in *Mississippi Today*, Ole Miss Who's Who Selection for 2018/2019, Ole Miss Greek Man of the Year 2019, a Commencement Highlight-*Beating the Odds*, and a feature in both *Mississippi Works* and *Mississippi Business Journal*. With so many recognitions under my belt, I continuously raised the bar for myself and moved forward to gain experience in STEM field.

My first true encounter with STEM in college was applying for a work study position as a research assistant in Dr. Nicole Ashpole's Pharmacology/Neuroscience Laboratory. This position granted me the opportunity to actively use science I was being taught and learn science that was not being offered in the classroom. With no idea what a Ph.D. was, the opportunity to work for her is one of the main reasons I chose to pursue a doctorate in Pharmaceutical Sciences and a career in academia. For three years, I worked as a research assistant in Dr. Ashpole's lab learning how to culture neurons and astrocytes, genotype, western blot, immunohistochemistry, stereotaxic injections, harvest, but most importantly, how to do science the ethical way. As one of her mentees, I received my own project where I presented a poster at Mississippi Academy of Science. I received 5th place out of 208 posters and a 2nd place oral presentation award. I also presented a poster in the Rotunda for State of MS Legislature to bring awareness of the funding that goes into public institutions for STEM and the product of their decision-students like me. Similarly, I gave an oral presentation for 50 Congressional Washington D.C. delegates. My most recent presentation was at the largest minority conference in the United States, the Annual BioMedical Research Conference for Minority Students (ABRMS) where I gave an oral presentation to an audience of over 100 and received a travel award.

Being a member of the Ashpole lab for over three years did not stop me from gaining experience in other disciplines. As a sophomore, I was selected to participate in the International Experience for Students (IRES) funded by the National Science Foundation under Dr. Jason Hoeksema and Dr. Jordan Zjawiony. My role during the six weeks in Poland consisted of field research, plant and fungi natural product extraction, PCR, and studying/identifying ectomycorrhiza fungi. Gaining experience in pharmacology and pharmacognosy disciplines, I decided to try biology/ecology research. Recently, I was a member of Dr. Jason Hoeksema's laboratory. My role consisted of collecting data from hundreds of scientific articles on arbuscular and ectomycorrhiza fungi creating a database that is being used for various meta-analyses. Luckily, I was able to find my passion at an early age while exposing myself to other environments. Undoubtedly, I am most passionate about the pharmacological aspects of research and integrating it with neuroscience. Psychological and neurodegenerative diseases are diseases that drastically affect our population. Personally, I would like to strengthen the field of these diseases and ideally find a way to treat them effectively. I know this is dreaming big, but I must start somewhere just as those before me did.

Outside of the scientific area, I worked as a junior excavator at an archaeological dig in Clinton, Mississippi. Our goal was to remove remains of unmarked graves from the 18th and 19th century and prepare them for relocation. Being a member of the Classics department, I studied abroad in Italy studying Latin and Roman archaeology. Thirdly, I traveled to Greece with my advisor, Dr. Aileen Ajootian, to study Greek pottery. I also studied abroad in the Caribbean Islands to learn about island formation, immigration, and extinction of species. These were all highlights

of my undergraduate career; however, my most admirable tasks were those impacting the community.

Service is one of my core values. Helping others and making small impacts in communities can be life changing. I served in various capacities within the last four years. Most recently, I was a member of the UofM MOST conference panel and served as the keynote speaker for the Division of Outreach first-generation college student program and as the keynote speaker to Panola County Sigma Beta Club. All three of those experiences allowed me to inform students on being an African American, a first-generation college student, breaking barriers, and becoming a successful college graduate. I have also traveled back to Morton High School where I graduated from to give a speech on how to get to college. Bringing an awareness of opportunities to those who are from disadvantaged backgrounds is one of my main focuses on how to broaden community service and inspire future generations to follow.

Within the past years, I have served as an Ole Miss ambassador giving tours to incoming college students and high school students; taught STEM club at Bramlett Elementary; worked various competitions likes MATHCOUNTS, Science Fairs, Chess competitions, Quiz bowl, and Speech and Debate competitions; participated in numerous health awareness walks; volunteered for Relay for Life; been a member of Ole Miss Big Event; Highway Pickup, Oxford Intermediate Mentoring to young males, Halloween festivals and Fall festivals to ultimately gain over 250 service hours. I strongly believe that my impact in the community has far exceeded my peers but it does not stop here. As a graduate student, I will be serving as the Community Outreach advisor for my undergraduate fraternity, I will continue giving tours for the University, and I will continue volunteering for Competition Corps. Serving others is a mandatory part of my life, and I plan to continue serving those around me. As I strengthen my educational background, I hope to start an after-school program for minorities to increase exposure to STEM research. With my service, I dream to make an impact in communities that are often forgotten while diversifying STEM.

As a first-year graduate student, I believe my journey has gotten off with a great start. My three years of research in the Ashpole lab has led to a submission to Journal of Neuroscience (under review) This year, I will be attending my first neuroscience conference (SFN-2019) where I received the Trainee Professional Development Award (an award is given to an undergraduate, graduate, or postdoctoral student who exemplifies scientific merit and excellence in research). Additionally, I was awarded the University of Mississippi Institutional Southern Regional Educational Board Fellowship (SREB). The University of Mississippi awards up to six fellowships per academic year for graduate students pursuing doctoral degrees who are seeking a career in academia. Beginning my graduate career with a well-known fellowship and an award from the largest neuroscience conference in the United States puts me in an amazing position for furthering my education.

Advancing the world with mentoring, serving my community, actively teaching, and actively learning are opportunities as a graduate student. Building upon the work that was done before me, I hope to advance science throughout my time in graduate school in small steps. Humbled by not receiving the GRFP award as a senior undergraduate, I can now say as a first-year graduate student, this award will extend my education in ways that I did not understand before. Receiving the GRFP will allow me to be a beacon of hope for those around me. As one of the few African American males in the pharmacology division, I hope to lead the charge in diversifying the field. Becoming a trailblazer for my community would allow me to impact in ways I never imagined. To me dreaming is natural but dreaming big is learned. I have learned to dream big, and the GRFP will only help my dreams become a reality.

Research Proposal:

Introduction: Cell structure dictates cell function. In the case of astrocytes, the most abundant cell type in the brain, intracellular ion balance directly affects cell structure. These cells are critical for proper brain function and alterations in their structure is associated with several disease states. Until recently, studies on astrocyte structural function were limited by technological difficulties. However, the development of light sensitive ion channels now allows scientists to target specific cells using transgenic approaches to target expression of these channels in place. It is possible to assess the benefits and/or damages caused by astrocyte ion structure and balance brain regions of living animals. I suspect that inducing astrocyte swelling with anion influx will impair learning and memory, but while, cation influx will reduce swelling in mice and subsequently promote learning and memory.

Aim 1: Anion influx causes swelling of astrocytes due to an increase in intracellular chloride which hyperpolarizes the cells [1]. Transgenic mice expressing Halorhodopsin (NpHR2) specifically in astrocytes will allow for selective control of anions, like chloride, into the astrocytes of the hippocampus. Working memory of mice expressing NpHR2 in astrocytes will be evaluated with Novel Object Relocation Task (NOR)[2]. Immediately following behavioral analysis, we will assess changes in astrocyte structure. I would predict astrocyte swelling will be induced with NpHR activation and will correlate with working memory performance. Cohorts of young and old animals will be assessed, and we predict that across both age groups, swelling will be inversely correlated with behavioral performance.

Aim 2: Cation influx increases several functions including the controlled release of gliotransmitters [3]. We will assess whether astrocyte specific cation influx alters cell structure and ultimately learning and memory. Like aim 1, we will target the hippocampus during (NOR). Following behavior, astrocyte structure will be compared. In addition, gliotransmitter levels will be assessed to correlate with behavioral phenotypes. With aim 2, I hope to see how altering cation flux changes old astrocyte structure and function potentially promoting learning and memory to levels observed in young animals.

Aim 3: Neurons and astrocytes work together for proper brain function with astrocytes providing structural support, energy, protective signals, and barriers for toxins. A significant protective property of astrocytes is their ability to buffer toxic concentrations of glutamate. A swollen phenotype is associated with reduced glutamate uptake. To validate this, neurons will be grown with cultured CHR2-expressing or NpHR2-expressing astrocytes which will then either be overloaded with glutamate or deprived of glutamate in the presence of optogenetic stimulation. Afterwards, we will examine the survival rate of neurons. We predict that the activation of CHR2 will increase glutamate uptake/neuroprotection while NpHR2 will reduce neuroprotection.

Methodological Approach: To analyze cation influx of astrocytes, a young and old cohort of transgenic C57/B16 mice will be created using the tetO-tTA system to generate astrocyte specific channel rhodopsin (CHR2)[3]. Astrocytic anion influx transgenic C57/B16 mice expressing NpHR2 will be used to analyze the hyperpolarization of astrocytes in the hippocampus. NpHR2 has been previously placed under the control of Thy1 promoter to control neuron expression[1]. Using this same system except placing NpHR2 under a GFAP promoter will allow us to control astrocytes. Fiber optic implantation protocol will be adopted from studies that have successfully completed implantation[4]. Power analysis and sample size estimation indicates, 13 animals will be needed in each group to achieve a power of 0.8 with an alpha of 0.5. Young mice age will range from 3-4 months while old mice will range from 20-24 months. NOR, Novel Object Relocation behavioral task will be used to assess if working memory is altered with changes in ion flux. NOR will be conducted with 3 Familiarization trials, a novel location trial, and a final novel object trial.

Each phase of the experiment is conducted for five minutes each with a 5-minute intermission. From other literature, we determined to stimulate opsins for 1 minute during each trial at 10Hz. Opsins will be stimulated after the initial 30 seconds in the maze during each phase of the experiment. Following behavior, tissue will be removed for various analyses. Gliotransmitter analysis will be conducted on dissected hippocampal tissue submitted to our chemistry core for analysis using mass spectrometry and HPLC.

Statistical Analysis: Behavioral analysis in mazes will be acquired using Ethovision Software. Data analysis for all studies will be conducted using R Statistical Software for significance whether t-test or ANOVA. Discrimination index of novel location and novel object will be calculated (time spent at NL or NO/ (time spent at NL or NO + time spent at F3)) to assess working memory. $p < 0.05$ will be used to determine level of significance.

Cell Viability: Immunohistochemistry staining for GFAP and DAPI will be used to quantify the number and size of astrocytes. Confocal microscopy will be used for imaging. *In vitro* survival rate of neurons in the coculture study will be analyzed using live/dead viability staining using microscopy.

Limitations/Broader Impacts: Limitations include difficulties correctly implanting the fiber optic to activate the opsins. I have previously performed stereotaxic injections on mice in addition to conducting and analyzing NOR behavior, immunohistochemistry, and cultured neurons and astrocytes. I have watched our lab technician successfully coculture neurons and astrocytes and have even grown these cells successful myself. Our lab also has significant experience with viability assays. The use of GFAP as our swelling marker is limiting as GFAP expression is altered in individual cells. However, our light channel expression is also limited to GFAP expressively cells, so this will suitably stain the cells we have targeted. The NOR task is common; however, the validity of the test is discussed because the mice lack motivation, reinforcement, or punishment to complete the task and use of multiple brain regions. Barnes Maze may also be considered as it is predominately a hippocampal task. Ideally, new technology such as wireless optogenetics could allow me to conduct more test where a physical connection would not interfere. Despite the limitations, the broader impacts of this study and can aid the science community in deciphering aspects of astrocyte biology; learning and memory; the aged or inflamed brain. Until recently, astrocyte functions were largely unknown in the brain, and although we have come far, the importance of astrocyte ion homeostasis and its regulation of cell structure remain poorly understood. Due to advanced technology, I will be able to seek answers to these questions using transgenic mice and optogenetics to analyze astrocyte structure/function.

1. Ting, J.T. and G. Feng, *Development of transgenic animals for optogenetic manipulation of mammalian nervous system function: progress and prospects for behavioral neuroscience*. Behav Brain Res, 2013. **255**: p. 3-18.
2. Balaji, S., et al., *Adenoviral-mediated gene transfer of insulin-like growth factor 1 enhances wound healing and induces angiogenesis*. J Surg Res, 2014. **190**(1): p. 367-77.
3. Cho, W.H., E. Barcelon, and S.J. Lee, *Optogenetic Glia Manipulation: Possibilities and Future Prospects*. Exp Neurobiol, 2016. **25**(5): p. 197-204.
4. Sparta, D.R., et al., *Construction of implantable optical fibers for long-term optogenetic manipulation of neural circuits*. Nat Protoc, 2011. **7**(1): p. 12-23.

Intellectual Merit Criterion

Overall Assessment of Intellectual Merit

Excellent

Explanation to Applicant

The applicant is highly qualified and demonstrates outstanding dedication to scientific research. They have received SfN trainee and travel awards, and internal supplemental graduate fellowships. The applicant has also presented their work at national and regional meetings and to members of the state and federal government, and is co-author on a submitted manuscript. They have actively sought numerous learning activities, including overcoming the substantial challenge of attending and succeeding in college as an under-represented first-generation college student from a rural and isolated town. The research plan was independently developed, is logical and compelling, and is impressively detailed; it even includes a plan for statistical analyses, a power analysis for animal studies, and potential problems and alternative approaches. The reference letters are strong and support confidence that the applicant will succeed in graduate studies and as a scientist.

Broader Impacts Criterion

Overall Assessment of Broader Impacts

Excellent

Explanation to Applicant

This applicant is involved in countless outreach and engagement opportunities specifically geared toward fostering STEM engagement and participation of those from under-represented groups. They have also presented their research to broad audiences, including legislators in their home state and in Washington, D.C.

Summary Comments

Overall, this is an outstanding applicant. They have clearly planned their career path thoughtfully and are well-prepared to execute high-level scientific research and to continue contributing good to the scientific community for decades to come.

Intellectual Merit Criterion

Overall Assessment of Intellectual Merit

Good

Explanation to Applicant

Strengths: The proposed research project poses interesting questions, and the experimental approaches seem tractable. The applicant has significant experience in scientific presentations to a wide variety of audiences. Weaknesses: The applicant's academic preparation though good is not at a high level for this very competitive field of applicants. In the research proposal, experimental strategies are not well explained clearly and logically. Some basic concepts are explained erroneously in the proposal.

Broader Impacts Criterion

Overall Assessment of Broader Impacts

Excellent

Explanation to Applicant

Strengths: The applicant has exceptional experience in outreach and leadership and has aspirations to build on this experience to

influence the next generation of scientists. Applicant would serve as an excellent role model for students wanting to succeed in the face of adversity. Weaknesses: The research project, as proposed, seems not well thought out.

Summary Comments

The proposal carries possibilities of significant scientific impact and broader significance. The proposed research explores effects on learning and memory induced by anion flux-dependent astrocyte swelling. The rigor of the research proposal, however, seems low. The long term benefits of this application to promoting opportunities for diversity in STEM research are potentially very high.

Intellectual Merit Criterion

Overall Assessment of Intellectual Merit

Very Good

Explanation to Applicant

This is a first-generation applicant from an underrepresented and underprivileged background. He grew up in a rural community in Mississippi with limited opportunities and role models. The applicant gained multiple awards as an undergrad, mostly local awards. As an undergrad, his academic performance (GPA) is below average, on the lower end of my review cohort. He gained significant research experience for three years. This experience led to fellowships to attend and present at national meetings, like ABRMS. He has also presented in regional conferences. The applicant also describes other research experiences that may have enriched his background, but could also be interpreted as a lack of focus. This lack of focus can explain the relative low productivity compared with students that conducting research for 3 years as undergrads. It would not be unusual to see many more participations in national and international meetings as well as an abundance of regional and undergrad posters and oral presentations. The applicant has a manuscript submitted as third author. Personal statement and research project are well-written, clear and engaging. Project describes the manipulation of astrocytes to increase the influx of anions or cations followed by behavioral studies. Project has a solid hypothesis, clear aims and sufficient experimental details. Techniques used for assessing the consequences of altering ion influx are not the best available. It seems strange that the applicant did not describe his current research project since he has worked on it for several years, has preliminary data to show and could propose interesting ideas to follow up in the next few years. Support letters are very strong and describe a candidate with a unique background and exceptional potential. Application could have been more informative by listing academic and professional activities in the first page.

Broader Impacts Criterion

Overall Assessment of Broader Impacts

Excellent

Explanation to Applicant

The applicant has been highly involved in leadership and mentoring activities as an undergrad and is continuing with those activities as a grad student. The applicant used the leadership opportunities to support minority and underprivileged college students and to serve as a role model for students in his former high school. He also lists a large number of mentoring and outreach activities, including science fairs, math, chess, science and debate competitions, and several other activities. This candidate exemplifies the "walking the walk" regarding service and broader impacts. This is illustrated in his writing, where mentoring and service mesh naturally with the life purpose of the applicant. He even proposes to create programs, like an after-school program for minorities. In most applications this will read as lip service for the reviewers, but this applicant started an organization as an undergrad to bring together minority pre-med students.

Summary Comments

This is an outstanding candidate with an impressive personal journey from a small rural Mississippi town to first-gen college graduate and doctoral candidate. The applicant has extensive research experience, has exercised leadership positions, and has exemplified a life of service to his community. The concerns are below average academics, productivity and staying in the same lab that he trained as undergrad. It is easy to recognize his potential and the benefits to his community of supporting him, the concerns also weight in the final score.