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DISCUSSIONS

THE CASE UNDERGRADUATE RESEARCH JOURNAL

2007

VOLUME 2

-FEATURING-

Kitty Chen - Patric Glynn - Paul Hay
Benjamin Kreis - David Poerschke - Brooke Schepp
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DISCUSSIONS

THE CASE UNDERGRADUATE RESEARCH JOURNAL

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Discussions began almost three years ago with a small group of students who hoped to establish not simply a research journal, but a collection of inspired and insightful research that would incite discussion in their academic fields. Now we are at our second issue and are delighted by the growing interest we have seen in our academic community. *Discussions* has rapidly developed over the course of the past three years, and we are proud of our hard-working and cohesive editorial board, supportive advisors, and the continued submissions that showcase the quality of the undergraduate research here at Case Western Reserve University and beyond. We are thrilled to have received such a wide variety of thoughtful and creative submissions for this spring issue. We have been privileged to bring together several fields of study, ranging from Greek mythology to sickle cell disease and biomedical imaging.

We hope that by the time you have become acquainted with the articles in this journal you will agree with us that these undergraduate authors have distinguished themselves by the depth and rigor of their research. Several have already been recognized in their fields. David Poerschke, the author of "Parametric Study of a Nd: Yag Laser Beam Interaction with Graphite," received SOURCE funding to present his poster at the 25th International Congress on Applications of Lasers and Electro-Optics (ICALEO). Additionally, it is our pleasure to congratulate Shaan Gandhi, author of a comprehensive review piece on three pharmaceutical cancer therapies in our previous issue, and recipient of a 2007 Rhodes Scholarship.

We thoroughly appreciate the tremendous support we have received from the SOURCE office and the Student Media Board at Case Western Reserve University. Sheila Pedigo and Bethany Pope, in particular, have provided encouragement and assistance in too many areas to count.

Discussions information and digital copies of our publications may be found online at www.case.edu/source/journal. Now more than ever, we encourage students to consider joining our team on either the editorial board or the reviewing committee. The journal is at a period in its development in which its members will have a tremendous impact on its direction and quality. As work on next year's publication will begin shortly, now is also the time to submit articles for consideration. *Discussions* accepts research papers, review articles, and scholarly essays from all fields of study written by undergraduates. Please visit our website for additional submission guidelines and instructions.

The students whose work is published in this issue have initiated academic dialogue across numerous disciplines, and we do not doubt that they will continue to do so. We feel very fortunate to be able to share their work with you. Thank you joining us in this second annual celebration of undergraduate research.

Heather Greenwood and Sandhya Ravichandran
Editor-in-Chief and Managing Editor

Fucose-Dependent Differentiation and Gene Expression of Common Myeloid Progenitor Cells through Notch Signaling Pathways

-Charles Su-

Charles is currently a second year student at Case, pursuing a Bachelor of Science in biology and a Bachelor of Arts in psychology. Aside from his academics and research, he is a Resident Assistant for Juniper Residential College as well as a member of Koinonia Christian Fellowship. Charles's current career plans are to attend medical school and continue research in pathology and immunology.

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I must thank, first and foremost, Dr. Lan Zhou for her incredible patience, expertise, and guidance on my summer research project. I must also thank Lebing Wei for her daily supervision and invaluable assistance in carrying out lab procedures and techniques. In addition I would like to thank the SPUR program, its coordinators, and the HHMI grant that supported me to make this summer research project possible.

ABSTRACT

The Notch pathway is an extensively utilized, evolutionarily maintained regulatory system which mediates a wide range of fate decisions among multipotent precursor cells by inhibiting differentiation along one pathway while promoting self-renewal or differentiation along an alternative pathway. Notch signaling has been shown to affect haematopoietic stem cell (HSC) self-renewal and differentiation, T cell versus B cell fate specification, and myeloid cell differentiation. The diverse functions of Notch in vertebrates are facilitated by complex interactions between four Notch receptors and five Notch ligands, all of which are expressed by hematopoietic cells and stromal cells. Moreover, Notch signaling is modulated by genes such as *fringe* as well as two unusual types of *O*-linked glycosylation; the addition of *O*-linked glucose (*O*-glucose) and *O*-linked fucose (*O*-fucose). Our goal is to determine whether *in vitro* myeloid differentiation is regulated by Notch activation, and whether this is a fucose-dependent process. Specifically, we focused our research on common myeloid progenitor (CMP) cell differentiation and the dynamic change of Notch-targeted genes during Notch regulated myeloid differentiation that is modified by fucosylation.

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CMS Silicon Pixel Detector Calibration

ABSTRACT

The Compact Muon Solenoid (CMS) pixel group at Cornell University is building a silicon pixel detector test station that will model the revolutionary detection and data acquisition system designed for the CMS experiment at the Large Hadron Collider (LHC) at CERN. When fully implemented at the LHC, the detector's sixty-six million pixels will be able to track and time passing charged particles that result from proton-proton collisions happening every twenty-five nanoseconds. With parts of the Cornell test station apparatus already functional, we have begun to understand and optimize the detector's programmable settings that tune its performance. The success of these optimizations has been quantified by performing various calibrations, also being developed here, that will also be used at the LHC to ensure that the pixel detector is working properly and taking the most accurate data possible.

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Benjamin Kreis

Benjamin is a fourth year physics major at CWRU. He has participated in particle physics research with the Cryogenic Dark Matter Search (CDMS) group at CWRU and the Compact Muon Solenoid (CMS) group at Cornell University. The latter of these projects was supported by the National Science Foundation's REU program and is the subject of this article.

-Acknowledgements-

I would like to thank all of the members of the CMS pixel group for their commitment to this project and for teaching me so much. I am especially grateful to my mentor, Professor Anders Ryd of Cornell University, for organizing this project and guiding me throughout it and to Professor Karl Ecklund of SUNY at Buffalo for his direction and for always providing the right resources. I worked closely with Heng Li, a Cornell University graduate student, and would like to thank him for his frequent, helpful suggestions and for being a steadfast source of motivation. I would also like to thank Cornell University graduate students Jim Hunt and Souvik Das for passing on bits of knowledge on everything from C++ to Quantum Field Theory. I deeply appreciate all of the time spent by Professor Rich Galik of Cornell University in organizing the Laboratory for Elementary Particle Physics (LEPP) REU program; I would like to thank him for being interested in my education and making this powerful learning experience possible. This work was supported by the National Science Foundation REU grant PHY-0552386 and research co-operative agreement PHY-0202078.

Healthcare Access Implications and Psychosocial Effects of Sickle Cell Disease

-Kitty Chen-

Kitty Chen is a senior at Cornell University, completing her dual concentration in Cognitive Neuroscience and Inequality, and will be graduating in May. A Cornell Tradition Fellow and long-time advocate of women's issues, she plans on continuing the project she created and developed in East Africa, empowering young women and girls in the HIV/AIDS crisis, while pursuing healthcare disparities research. She has completed research appointments at the Yale School of Medicine, Cornell Weill Medical College, and New York Presbyterian Hospital. When not in the neuroscience laboratory or abroad doing service work, she enjoys being a theatrical performer for such productions as the Vagina Monologues.

-Acknowledgements-

I would like to give special thanks to Dr. Suchitra Acharya, MD and Dr. Donna M. DiMichele, MD at New York Presbyterian Hospital for taking me under their wings and allowing me to participate as part of the pediatric hematology and sickle cell chronic care clinic team for the fall/winter of 2006.This rewarding experience would not have been possible without you. Deep gratitude also goes out to Dr. Sam Beck, PhD, my professional advisor at Cornell Weill Medical College for his direction, inspiration, and continuing support. Each one of these mentors has imparted great wisdom and insight with their knowledge and understanding of biomedical ethics. I am grateful to have them in my life.

Millman (1993) defines healthcare access as “the timely use of affordable personal health services to achieve the best possible health outcomes,” implying that healthcare access involves only access to insurance, patient satisfaction with physicians, and/or patient utilization of preventive health care (p. 5). However, I agree more with Rouse (2004), who uses the term “access” more broadly, such that patient access has two parts. The first part, which has multiple variables, is a patient’s ability to be seen by a medical professional, and the second part is the quality of the patient/practitioner collaboration, which is affected by prior knowledge, communication, and professionalism. This second part has numerous cultural and social dimensions, and contributes significantly to racial disparities in health outcomes. The treatment of sickle cell disease can be very illustrative of our current access to healthcare issues in the development of patient services. One needs to realize that disparities in minority healthcare outcomes will not disappear if we simply base the idea of access on the existence and availability of health care services, as issues of unequal access today deal with more subtle matters. This paper will demonstrate the importance of physicians’ perceptions, communication, and understanding in provider-patient relations, as well as the importance of psychosocial interventions in the treatment of sickle cell disease.

Sickle cell disease is an autosomal recessive illness that primarily affects persons of African ancestry, Arabs, and those of Asian ancestry. However, perhaps in part due to insurance reasons, all of the sickle cell patients I have seen thus far in our Sickle Cell Clinic have been of African descent. This disease, though described as “rare,” in fact affects 1 in 400 or 500 African Americans in the United States

(Holbrook & Philips, 1994). The genotypes of sickle cell anemia are named for the regions of Africa from which the original gene migrated, and are each thought to impart a different natural history of clinical expression (Holbrook & Philips, 1994). Many physicians find sickle cell disease difficult to treat. For one thing, the intensity of an acute sickle cell crisis can be so severe that it has been qualitatively compared to terminal bone cancer pain. However, because pain is subjective and immeasurable, the patient, rather than somatic distress, is often thought to be the "problem." Moreover, there is no obvious precipitating factor for a painful (acute vaso-occlusive) crisis, which can and does occur without objective physical signs (Sutton, 1999).

While in the past the disease was a metaphor for blood or race pollution, currently sickle cell pain is a metaphor for social dysfunction and the lack of self-control in the African American community (Chestnut, 1994). Thus, although acute, recurrent, painful episodes are often the predominant feature of this illness, sickle cell disease is not one-dimensional. The frequent use of narcotics to treat severe pain leads to drug dependence in some patients, which results in their stigmatization by some health care professionals. The majority of sickle cell patients are African American, and when sickle cell patients enter the emergency room asking for strong opioids, the overwhelming response by physicians is to view them as "drug-seeking and difficult to manage"—both medically and socially (Rouse, 2004, p. 371). Shockingly, this perception is so pervasive that many hospitals try to dissuade sickle cell patients from seeking care in their facilities and refuse to establish affiliated sickle cell clinics.

For many patients with sickle cell disease, pain is a part of their daily lives, and this can indeed lead to misuse of the opioid therapy prescribed. Such misuse, in turn, can lead to tolerance, dependency and overutilization of hospital services—but this is a very small subset of sickle cell patients. Much like (and perhaps in part due to) racial stereotyping, these patients are labeled as "drug seekers," and can induce the staff to form false beliefs about all sickle cell patients who come to the Emergency Room. This kind of stereotyping carries over and interferes with the quality of pain treatment for other sickle cell patients.

As Sutton, et al. (1999) states, "the failure by healthcare providers to distinguish between addiction, dependence, and tolerance is a major component in the failure of effective management of the sickle cell patient with pain" (p. 284). Such misunderstanding can lead to negative provider-patient relationships and conflicts, and would thus feed into a vicious cycle in sort of a self-fulfilling prophecy, where future patients do not get the pain treatment and care they need, act and voice out of frustration, are seen as "bad" sicklers, reinforce a provider's stereotype due to his/her lack of understanding of the disease, and thus further negatively influence the provider's future interactions with sickle cell patients. One devastating example of the consequences of this type of misunderstanding and "drug-seeker" stereotyping is described by Rouse (2004) in recounting an interview, where a resident refused to check on a girl whose parents were trying to communicate that something was not right. The resident also refused to call the attending physician, and reportedly slammed the door in the mother's face. The teenage girl died of a morphine overdose that could have easily been prevented if the resident had checked on the patient or had called the attending. On a different level (that which the resident's perceptions and reasoning lies), the tragedy could have also been avoided if he believed that sickle cell patients suffer—at least as much as cancer patients do. It was likely that the resident instead viewed sickle cell patients and/or African Americans as drug seeking, and therefore treated the morphine he prescribed like a fix for the patient rather than a treatment for her pain.

When I look at my time at the Pediatric Hematology Clinic and the sickle cell services that we provide, I cannot help but feel a sense of pride in the stark contrast that I have experienced first-hand. Dr. Acharya, for one, is very understanding when it comes to a sickle cell child's pain crisis, and makes sure that the parent has pain medications on hand at home in case there is a need to alleviate suffering. I have yet to experience how these patients are treated in the ER or as inpatients when they come in for serious pain crisis episodes or fevers, but I do know that Dr. Acharya goes on rounds and attends to these patients to ensure they are taken care of outside the outpatient clinic as well. Perhaps there would be more prejudices and difficulties visible when it comes to the adult sickle cell sufferers, but I have yet to have any reason to believe this at New York Presbyterian Hospital. From what I have garnered from the Pediatric Sickle Cell Clinic model at New York Presbyterian, I wonder if the best approach to understanding the origins of myths and misconceptions, stereotyping and stigmatization that surround blacks and sickle cell disease would be to cast away bias (including those that are subconscious or not overly overt) by employing empathy and focusing on the issues of pain and pain management.

Ethnocultural factors will impact on our subjective (individual) experience, cognitive, and physical reaction to disease, and one's perception of how these ethnic and cultural factors impact their experience will in turn shape cognitions (including beliefs, values, attitudes) that guide, direct, alter, and motivate behavior (Chestnut, 1994). Results of Chestnut's 1994 study on perceptions of ethnic and cultural factors in the delivery of services in the treatment of sickle cell disease show that race was perceived as the most influential factor in healthcare delivery. Both medical staff and family respondents consistently viewed whites as getting better service than blacks. If blacks perceive whites as getting better service simply because they are white, it might create a feeling of "second class citizenship," which could easily result in resentment toward the medical system and the healthcare process. This resentment may translate into lateness and cancellations, noncompliance, miscommunication, and hostility in interpersonal relationships with medical staff—all factors that delay and inhibit access to quality healthcare.

Since routinized procedures, or protocols as we at New York Presbyterian Hospital call them, often ignore "the human element" in treatment and may not provide for the broad physical and psychological needs of the patient, health care professionals usually assess the situation from their own perspective and proceed with treatment based solely on those perceptions in an attempt to render services (Ahmad, 1989). However, from what I have observed during my clinical rotations across different specialties, the most effective treatment would appear to occur when the patient/parent is actively concerned and involved in the patient's treatment and experience. Empathy and compassion on the part of the provider plays a major role in the provider-patient alliance in arriving at the most effective treatment, as I feel making an effort to gain information of the patient's perspective will influence utilization, compliance, appointment keeping, overall responsiveness to treatment, and psychological reactions to the illness (something that is especially important when it comes to pain management). The need for such information becomes even more crucial when delivery of service is to ethnically, culturally, and/or socio-economically diverse individuals, who may have ideas about healthcare that are very different from those of the providers ("Unequal Treatment," 2003). Understanding the individual from his/her own frame of reference, also known as the "phenomenological approach" becomes so important because, as psychologists assert, behavior evolves from cognitive processing of what they believe and perceive the situation to be and the action taken (Hanna, 1973). This reality, or realities, becomes powerful in governing behavior—including that of healthcare practitioners. Thus, I believe the physician who truly empathizes with a patient will actively provide the best possible care for the patient, regardless of the patient's background, race, or socio-economic status.

In my experience with the Sickle Cell Clinic at New York Presbyterian, I have also found that good communication is important for quality care, and providers must make an active effort to ensure they are communicating with patients. Healthcare professionals need to understand that coming to the clinic may have many negative aspects for patients, but a staff, such as Dr. Acharya or a nurse, that is seen as friendly, caring, and concerned helps to mitigate the experience. In contrast, poor communication can result in suspicion and mistrust. Understandably, many blacks feel they stand outside the medical system and are skeptical of opening themselves to it ("Unequal Treatment," 2003). "Not understanding" is sometimes a form of resistance to something someone does not trust or want to accept. However, perhaps due to the quality of care that we do indeed provide, I have yet to have seen this type of resistance on the part of the patient or parent during my time with the clinic.

In addition to good communication, compassion is also an important quality I feel good physicians should learn to employ in dealing effectively with sickle cell patients. According to a study by Robbins (1997), nurses' perceptions of sickle cell patients, with few exceptions, were overwhelmingly negative, in contrast to their expressions of sympathy with their cancer patients. Specifically, the study documents that overwhelmingly nurses and residents think sickle cell patients exaggerate their pain significantly more than patients suffering from seven other illnesses. As a result of these perceptions, practitioners treat their pediatric sickle cell patients with lower doses of pain medication in comparison to their cancer patients with similar symptoms. The lack of compassion as an impediment to healthcare access is further illustrated in the following narrative:

> There were at least three other staff members who validated the perspective of the social worker and who expressed concern about the quality of sickle cell patient care, the lack of compassion, and the use of diagnostic labels to limit patient access to health care. These institutional practices […] were the result of racism (Rouse, p. 380-381).

Thus, if a staff member harbors prejudice about a patient (whether or not it be conscious, overt, or aversive), he/she will most likely continue to employ what is considered medically sound healthcare, making this decreased "access" harder to detect. This is why we must look at how healthcare decisions are rationalized to identify how prejudices may influence knowledge, and examine instances when physicians sometimes unwittingly mask hegemonic discourse about race/ethnicity, class, and gender in treatment decisions, or when physicians cloak insurance mandates in the guise of rational medicine (Bloche, 2001; Daniels et al. 1999).

In addition to equalizing access via changing healthcare personnel attitudes and perceptions toward sickle cell patients, one must also consider the need to provide external healthcare services that dictate and impact what happens at the clinic—and sometimes even whether or not the patient comes to the clinic in the first place. Since many sickle cell sufferers are from a lower socio-economic group, healthcare providers must understand how transportation problems, economic problems, or daycare problems greatly influence utilization of, and hence access to, medical services.

The availability of emotional and social resources is also crucial, since the individual's experiences with episodic pain crises could often affect the emotional life of the patient (Ohaeri, et al., 1995). For instance, sickle cell patients have been shown to experience high levels of anxiety in regards to their illness (Chestnut, 1994). Other challenges associated with sickle cell disease that can result in psychosocial difficulties include growth retardation, behavioral problems, learning problems, and possibly a decreased IQ compared to their peers (Malach, et al., 2002). Moreover, sickle cell disease children are more likely to report social impairment such as restriction in their play and domestic activities, feeling inferior to others, having bad luck, fear of under-achievement in life and fear of potential early death than both the control groups with bronchial asthma and with some acute medical illness (Tunde-Ayinmode, 2005). One needs to understand that social issues like educational attainment, employment status, and social networks are important determinants of illness course and care-seeking behavior.

Here, we see the benefit of building support systems such as sickle cell self-help and support groups. However, though I see Dr. Acharya briefly addressing these concerns during the examination, I think these patients would benefit if a more comprehensive, multidisciplinary, division-of-labor- approach was implemented. As Trzepacz, et. al (2004) suggests, vigorous screening programs for mental health programs should be included in the routine care of children with sickle cell disease, and psychosocial intervention research should be implemented to ameliorate problems for the children at greatest risk. Comprehensive sickle cell programs have played a role in the reduction of morbidity and mortality "by providing easily accessible healthcare services administered by individuals knowledgeable about the disease and its complications" (National Institutes of Health, 1995, p. 5). Ideally, I believe that a comprehensive care clinic, much like the hemophilia clinic I have been participating in, consisting of hematologists, occupational therapists, social workers, psychiatrists, and specialized nurses, would enable one to provide early diagnosis, preventive health maintenance, early treatment of life threatening complications, and development and implementation of new treatment modalities for young sickle cell patients. This multidisciplinary approach, where bio-psycho-social issues are dealt effectively under one umbrella, not only allows whole teams to efficiently work together with the patient to reduce morbidity and mortality, but also do so while increasing quality of life psychosocially. This, to me, is true access to healthcare.

I hope that this paper has conveyed the point that "access" to healthcare may have a far broader meaning than simply having insurance and/or the ability to pay. Access can be translated to the lack of an adequate amount of medical professionals who can help to create a feeling of empathy and belonging, to social and health policies which often do not include adequate numbers of multiculturally competent persons in the policymaking process, to funding for research and facilities which most often reflect a disproportionate concern for issues of minority health, and even to provider-patient communication. Thus, treatment programs that are going to be effective in treating ethnically and culturally diverse individuals indeed must stress open communication, convenience, ethnic and cultural sensitivity, caring, and concern—qualities that I have seen firsthand with Dr. Acharya in dealing and interacting with sickle cell families.

Physicians construct access based upon moral perceptions of the patient and determinations of what constitutes a life well lived. Coupled with the lack of knowledge about sickle cell disease, one of the problems with sickle patients is that health care professionals make a connection between African Americans using drugs and existing negative stereotypes. If ease of access and understanding of the medical system are so crucial, there is also a need for broader education and exposure to the medical system for patients in times other than medical crisis, such as for much-needed psychosocial services. It is apparent that more research needs to be done in an effort to explore how patients feel their ethnic and cultural characteristics influence the availability and quality of healthcare service they receive.

Not many people will view qualities such as empathy and compassion as means of achieving objectivity with patients, but I argue that these are important skills to employ when one wants to give the best possible treatment one can to his/her patient, unfettered by racial, cultural, or socio-economic stereotypes or stigmatizations that exist. To do otherwise will mean that one is not providing true equal access to healthcare. I firmly believe that education, research, multicultural competence and sensitivity, as well as hands-on experience, resulting in changes in attitudes and behaviors, will ultimately lead to a more empathic approach to the sickle cell patient.

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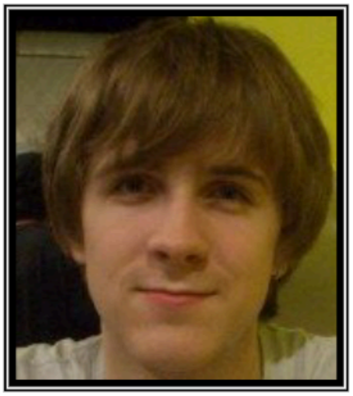
Alternative Methods to Autologous Nerve Grafting for the Regeneration of the Peripheral Nervous System



-Patric Glynn-

Patric Glynn is a second year student at Case pursuing a major in Biomedical Engineering in the bioelectric sequence as well as a minor in Electrical Engineering. His research interests include rehabilitation studies involving neural prostheses and functional electrical stimulation. After graduation, he plans on attending either medical school or graduate school.

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INTRODUCTION

The peripheral nervous system is made up of the nerves and neurons that are outside of the central nervous system. These nerves and neurons are used to transport information between the brain and the rest of the body, and when damaged, can severely impact an individual's motor and sensory function [1]. In the United States there are more than 50,000 surgical operations performed each year to repair peripheral nerve damage [2]. When cut, peripheral nerves attempt to grow towards and reconnect to the tissue or muscle they had previously controlled [2].

Neurons are able to effectively regenerate over short distances without any help. However, when the gap they must regenerate across is too wide, a graft is needed to guide the neuron and to prevent the formation of a neuroma [3]. Regeneration is most successful when the severed axons are able to successfully grow through the remnants of the site where the original connection was. In order to help aid in the regrowth of longer gaps a technique called "nerve grafting" is used [4]. Without such grafts, these injuries may never fully heal, and can be permanently debilitating. With the use of these grafts, a much more successful recovery is possible.

Autologous grafts, with their high rate of success, are currently the method most in use today for such situations. However, there are drawbacks to using this method. Autologous grafts require that a nerve be taken from somewhere else on the patient's body. Not only must the patient have an additional operation in order to obtain this nerve, but the patient also must consider a possible loss of function at the location from which this nerve was taken [4].

Because of the drawbacks associated with this method, alternative types of grafts including collagen and non-neural grafts are currently being examined to replace autologous nerve grafting as the primary method of assisted peripheral nerve regeneration. The purpose of this paper is to review the positive and negative aspects of autologous nerve grafting, summarize the capabilities of other forms of grafting to replace the current method, and to present concluding thoughts on the future of peripheral nerve grafting.

AUTOLOGOUS NERVE GRAFTING

The primary method of peripheral nerve grafting in use today is the autologous nerve graft. In this treatment, a comparable nerve is first removed from another part of the patient's body. The nerve is then used to bridge the gap and connect the two ends of the severed nerve, and to then guide the regrowth of the actual nerves [5].

There are several reasons why this method has become so universally accepted. One reason is that by taking the donor nerve from within the patient's body, there is no chance for immunorejection. This is a major benefit of autologous grafting as it nullifies a significant portion of the risks associated with implanting a foreign material into a patient's body. The autologous graft also has a fairly high success rate, and usually restores the majority of functionality to the damaged location. This graft also provides a support structure that promotes regeneration [6].

However, the use of the autologous graft as a nerve grafting method is not perfect, and there are several disadvantages. The most prominent disadvantage to this method is the possibility of a loss of function at the site where the donor nerve was taken. By removing a nerve from a fully functioning part of the body, there is the risk that full functionality at this location will be lost. In addition, the patient may have complications from the additional surgery, and is subjected to an increased risk of infection at the donor site. This method also can lead to incomplete regeneration of the damaged nerve, even with the use of the autologous graft [2].

Another detriment to autologous grafts is that there are a limited number of locations that can be used as a donor site, as the selected nerve must have a similar structure to the nerve that was removed. In addition, another negative outcome is the possibility of the death of the donor tissue because of an unsuccessful attempt to attach it to the damaged location [5]. With this complication, the patient would be left with two damaged locations and no restoration of function in the original location.

NON-AUTOLOGOUS NERVE GRAFTING

Attempts have been made to discover a method to assist in peripheral nerve regeneration without involving tissue removed from another location on the patient's body. To eliminate this requirement, graft methods have been created that involve the use of extracellular matrix (ECM) of non-autologous tissue instead of autologous tissue [4]. However, there are disadvantages with the use of nonautologous tissue. The cells native to the non-autologous tissue must be completely eliminated in order to remove the risk of immunorejection, and this is difficult to do without the destruction of the ECM [6]. If the tissue is to be used as a nerve graft, it is vital that the ECM remain intact.

The extracellular matrix, or ECM, plays an important role in nerve regeneration. The ECM is the material that surrounds cells, and molecules within the matrix can help guide, promote, or inhibit the growth of neurons. It may be necessary to emulate the ECM in order to accurately guide the axonal regeneration. Attempts have been made to create a non-neural graft that satisfies all of the criteria above. However, it has been difficult to create a graft that maintains the structure of the ECM while eliminating cellular debris because of limitations when using thermal, radiation, and chemical treatments, and because of this, bioartificial grafts have had lower success rates than autologous grafts [1].

There are a variety of techniques used to create a graft using non-autologous tissue. These techniques include thermal, radiation, and chemical treatments, but thermal is the most common method in use today [6]. When tissue is subjected to thermal treatment, it goes through a series of freeze-thaw cycles. These cycles kill the cells in order to make the graft acellular, but they damage the native ECM and do not extract the cellular debris from the tissue [2]. After this graft is implanted into the patient, the cellular debris left behind must then be cleared out by the patient's immune system before regeneration is able to begin [6]. Radiation treatment does not destroy the extracellular matrix to the same extent, but it also fails at extracting the cellular debris from the material. Because of the presence of drawbacks in both of these creation techniques, it is difficult to create a graft that successfully removes cellular debris while leaving the ECM intact.

Chemical treatment is able to effectively wash away the cellular debris, but it also causes significant damage to the ECM. However, recent advances have created chemical treatments which are able to effectively wash out cellular debris while still leaving the ECM largely intact [6]. Because of these advances, chemical treatment may be able to one day replace thermal treatment as the primary method of decellularization and be much more successful at leaving the extracellular matrix intact.

NON-NEURAL NERVE GRAFTING

The first type of non-autologous graft that will be discussed is the non-neural, or bioartificial, nerve graft. The use of this graft attempts to avoid the disadvantages presented by the autologous graft, while still promoting peripheral nerve regeneration. In order to achieve this result, the graft must be made out of a material that has similar characteristics to that of the nerve it is guiding. In addition, the graft must also be biocompatible and biodegradable in order for the graft to be considered a fully acceptable placement [3].

Bioartificial grafts use nonautologous tissues and make use of the presence of both Schwann cells, which guide the neuron regrowth, and extracellular matrix. These grafts must both bridge the gap caused by the patient's injury and help promote the regrowth of neurons across this gap. The extracellular matrix of the nonautologous tissue may be the main component of the graft used to improve the regrowth of neurons [7].

One method of increasing the effectiveness of an artificial material as a functioning nerve graft is to seed it with Schwann cells. Schwann cells are myelin producing cells required for axonal regeneration by guiding the axons and producing adhesion molecules [6]. Without the use of Schwann cells it is much more difficult for neurons to regenerate across long gaps. In the most effective experiments that involve collagen as the nerve graft, Schwann cells were seeded within the collagen in order to promote growth [5].

COLLAGEN NERVE GRAFTING

Another alternative to the autologous nerve graft that is being developed is the use of a collagen mold to create a graft between the two severed ends of a nerve. Collagen is one of the major components that make up the extracellular matrix. This material has had a large degree of success in other types of surgical procedures, and has also been used in nerve repair [4]. It is a viable material for use as a graft as it provides a high level of permeability when placed within the body, is biodegradable, and allows different cell types to grow within it [4].

What makes collagen even more useful as a nerve graft is that it can be shaped in structures that are able to promote nerve regeneration [4]. Collagen itself actually plays an important role in nerve regeneration, and it is possible to control the porosity of collagen structures. This control makes it possible to decide the environment in which the nerve regeneration takes place [5].

COMPARISON OF METHODS

At this point in time, the autologous nerve graft has had the highest success of nerve regeneration. The complications involved with an autologous graft make it desirable to find a method that could replace it. Results from experiments conducted by scholars such as Felix Stang, Hisham Fansa, Gerald Wolf, and Gerburg Keilhoff indicate that collagen does not appear to be an acceptable material to use as a nerve graft [4]. In their 2005 experiment, the authors were able to obtain slightly better regeneration rates by adding Schwann cells to the collagen grafts than they were by using the collagen grafts alone. Even when using the Schwann cells, however, the regeneration capabilities of neurons within a collagen graft is much lower than if an autologous graft had been used. This finding leads to the conclusion that while collagen grafts may not be an adequate replacement to autologous grafts, the presence of Schwann cells appears to be able to improve the regeneration rate of neurons in non-neural grafts, and another type of graft may therefore be enhanced with such cells.

In contrast, another experiment conducted in 2003 by Yueh-Sheng, Chien-Ju Liu, Chun-Yuan Cheng, and Chun-Hsu Yao entitled “Effect of bilobalide on peripheral nerve regeneration” resulted in a very different outcome when using collagen as a nerve graft. In this experiment, the researchers attempted to combine collagen with laminin, a neural growth stimulant, and fibronectin, a water-binding protein to create their graft. They then attempted to combine this graft with bilobalide, an extraction taken from *Ginkgo biloba* leaves. They found that this mixture significantly promotes peripheral nerve regeneration, but that it is crucial to use the correct dosage of bilobalide, as a large dosage can actually inhibit growth, and a dosage that is too small would not be effective [8].

Non-neural grafts appear to have potential as a replacement method to autologous grafts in the near future. With the development of improved methods for preparing nonautologous tissue along with other improvements associated with additional experimentations, non-neural grafts may be able to reach the same level of success or perhaps even surpass this more traditional form of grafting. Because non-neural grafts do not seem to have the disadvantages that are associated with the autologous graft, they could easily become the method of choice for peripheral nerve regeneration, once equivalent success rates are achieved.

SUMMARY AND CONCLUSION

As of this point in time, autologous grafts are the most widely used form of nerve grafting. These grafts have a higher success rate compared to other grafting methods being developed, but drawbacks associated with this graft type make it desirable to develop alternatives. Experiments involving collagen as the base for a nerve graft have shown that this method is probably an ineffective form of treatment for the regeneration of peripheral nerve cells. However, these studies have also shown that there are benefits to imbedding Schwann cells into implanted grafts.

It has become hard to make any further advances with collagen as the base for nerve grafts, as it is difficult to remove the drawbacks inherent in using collagen as the base for the graft. The collagen tubes' wall thickness, porosity, diameter, and alignment of the inner skeleton must all be manipulated in order to produce a good alternative for nerve grafting [4].

Even with the manipulation of these factors, animal studies that made use of collagen grafts for nerve repair showed a permanent loss of motor function and impaired sensitivity. In general, very few myelinated fibers are able to regenerate through a collagen conduit and enter the distal nerve segment, even when Schwann cells are seeded in the graft to increase the regeneration abilities [4]. Importantly, collagen grafts that made use of Schwann cells did have an increased regeneration rate, but this rate is not achieved to the point that it is comparable to the regeneration rate of autologous grafts. In the experiment involving bilobalide, it appears to be difficult to correctly manipulate the bilobalide dosage in order to effectively create a nerve graft that would ever surpass the success rate of the autologous graft. Differences in suture size and extent of the damage would make it difficult to judge the correct dosage of bilobalide, and the results would end up being less predictable than the current method.

In contrast, non-neural grafts appear to have a significant chance at becoming the dominant grafting technique. Recent advances in development techniques involving the treatment of tissues with chemicals for non-neural grafts have been developed that leave the native ECM intact while removing cellular debris [6]. If this new technique is refined even further, it may be used to create a material that is viable for use as a nerve graft. It may then be possible to increase the success rate of the graft by seeding the inside of it with Schwann cells. This combination may be able to lead to a grafting device that has a similar success rate to that of autologous grafting but without the drawbacks associated with an autologous graft.

The benefits to using tissue not taken from the patient's body remove the complications associated with the autologous graft, including the additional surgery, the limited availability of donor nerves, and the possibility of a loss of function at the donor site. Various advantages and disadvantages associated with each of the methods described in this paper are summarized in Table 1.

As can be seen in Table 1, when the advantages and disadvantages of autologous and non-neural grafts are directly compared, as shown, it is evident that if non-neural nerve grafts are able to obtain a success rate comparable to that of the autologous nerve graft, it could easily replace autologous as the most used method for peripheral nerve regeneration.

It is clear that while the autologous nerve graft is the most popular method in use today because of its high rate of neural regeneration, there are still enough drawbacks that make it desirable to find an alternative. The most promising alternative at this time appears to be the non-neural graft. This type of graft has the potential of a high success rate with none of the drawbacks currently associated with the autologous graft.

Method	Advantages	Disadvantages
Autologous	High success rate, no chance for rejection	Additional surgery, possible loss of function at donor site, chance for infection at donor site, limited donor site locations
Non-neural	Only one operation, low to no chance for rejection, few complications	Currently not as high success rate as autologous, must treat to make acellular
Collagen	No chance of rejection, easily obtained materials	Low or unpredictable success rate

Table 1: A Comparison of Grafting Methods for Peripheral Nerve Regeneration

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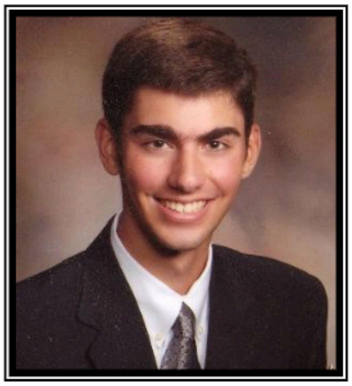
Mythology and Astronomy as Manifestations of Ancient Greek Culture



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It is common to think of mythical heroes as being "larger than life." The stories of their legendary pursuits put these warriors on a level above that of the mere common man. The cosmic insignificance of the normal human being is also suggested through the study of astronomy. One cannot help but feel like an insignificant speck floating through space when one approaches the magnanimity of the night sky. Thus it is no surprise that many of the ancient star watchers graced the names of the constellations with those of the heroes of their mythologies. However, it is imperative to remember the human element in both of these pursuits. Stories do not exist without storytellers, and astronomy cannot be studied without astronomers to do it. No matter how much evidence exists showing that the Trojan War really happened, still it is Homer who made the myth what it is today. Similarly, even if a cluster of stars looks exactly like a horse, it takes an astronomer to give it the name Pegasus. Both mythology and astronomy are thus profoundly affected by the cultures of which the mythmakers and the astronomers were a part. The Greek hero Perseus provides one such example of this connection between mythology, astronomy, and culture, and since his legend was well known since at least the seventh century B.C., he is also one of the oldest such examples (*Masks* 83). The mythological story of Perseus and its subsequent astronomical associations contain reflections of cultural fears and values for the ancient Greeks.

The Perseus myth provides a valuable example of the ideal Greek man. Martial valor was one of the highest virtues of the Greek society; Victory itself was even deified and honored with a temple in the Acropolis. Because of the importance of warfare in defending the Greek way of life, becoming a worthy fighter was an important step in the lives of many young Greek men. Perseus thus sets the bar: "The mass of men appreciate and pay homage to the courage and sacrifice of the warrior, defender of home and country. The hero's risk is therefore the source of his nobility and subsequent privilege. Thus if they wish to uphold their claim to nobility and its rewards, it is their duty to fight" (Hatab 74). The Perseus story "has clear characteristics of an initiation myth: the hero travels to marginal areas to get his special weapon that commands death" (Bremmer 27). But in a very broad way, this story also is a battle between the forces of good and the forces of evil. In it, "the individual heroes become more significant than groups of combatants in symbolizing the victory of virtue over vice, since this war is one that every soul must wage alone" (North 29). This has an astronomical suggestion: "some myths involving male heroes…have a mystical core in solar symbolism: for instance, Perseus's struggle against the Gorgons is a battle of the solar cult against the forces of darkness" (Blok 44). The principal vice for the Greeks was hubris, a word that suggests overbearing pride or arrogance. The Perseus story warns against having hubris: "the sea serpent is sent as a consequence of Cassiopeia's vanity, and Perseus's confrontation with the Medusa results from his hubris in boasting to Polydectes of his valor" (Slater 332-333). This legend also teaches the importance of xenia in Greek culture. Xenia was the virtue of hospitality; Greeks were expected to be kind and benevolent hosts to their guests, or any supplicants at their doors. In the Perseus myth, xenia is exemplified when the fisherman Dictys "does [Perseus and Danae] both reverence, takes them into his hut and passes them off as his kinfolk" (Kerenyi 48). Susan Langdon notes that Greek boys took part in an actual male initiation rite that recreated the Perseus story. As Perseus maintains social order through the slaying of monsters and evil men, so the story of Perseus maintains social order by instilling the cultural values of the Greeks into their young men in this initiation tale (Langdon). Men would wear Gorgon masks and fight young boys, who were required to "kill" the Gorgon (Langdon). The importance of this slaying is confirmed by the chosen pose of Perseus in his constellation: he is holding the recently slain head of Medusa. This physical example of martial prowess underscores the lesson taught by the Perseus myth.

The importance of religion in one's daily life is also a value instilled by the Perseus myth. It is necessary to state that "myths were not intended as 'speculation' or even mere stories because they were functional, woven into the concrete lives of a people. Myths established social and educational values; prescribed daily tasks and ceremonial responses…[and] gave meaning to birth, maturation, and death" (Hatab 20-21). The gods, then, were believed to come down to Earth not only in myths, but in everyday life as well. The Greeks set up temples to deities with the actual expectation that those deities would have a presence in the temples. In the myths, therefore, "various deities make regular journeys to their appropriate cult places. Heroic travels are equally purposeful, involving as they normally do some important trial or quest" (Pozzi 51). The Perseus myth, like most Greek myths, specifies many actual place names in Greece; the notion is conveyed that Greek heroes were just normal men elevated to greatness by their decisions. In fact, "all over the country were the shrines and tombs of the heroes and heroines of early days, who seem to have filled a part very much like that filled by the saints of the Christian church" (Woodward xi-xii). Thus Perseus is an example of how the ideal warrior can be immortalized in the stars despite being human. Perseus's religious significance also touches on the importance of genealogy to the Greeks. In a patriarchal and patrilineal society such as the one Greece had, one's parentage was an important factor of one's social status, and not just by considering one's immediate parents. For example, Martin Nilsson writes that in preparing their campaign against the Greeks, the Persians sent heralds to the Argives to dissuade them from taking part in the war because the Persians were descended from the Argives through Perseus (89). Also, the concept of the "divine right of kings," which gives a ruler authority over a people because of his divine lineage, was still being used by Greeks up until the beginnings of democratic stirrings in the sixth century B.C. Perseus is a hero with a social function, who is of divine descent but takes his place among mortals, who bears exceptional power and resources to rid the country of monsters, and who provides a genealogy for the nobility by marrying a king's daughter, winning glory and posterity (Blok 324-325). It is only fitting that the son of Zeus would rule over a people. Thus, the gods were expected to interact with Earth not only through themselves but also through their kin, the royalty of any given city-state. Perseus shows this distinction in the story because "the important position of the hero in later life within the community is thrown into greater relief by his earlier removal from that community" (Bremmer 44). Being godlike, Perseus is expected to take his place not only among the people but among the stars as well. His mythology shows the importance of religion in one's daily life.

The Perseus story also demonstrates the role of women in Greek society. The ideal Greek girl was called a parthenos. Young maidens were expected to be chaste and wholesome; they were to take their place in the home until marriage, at which point they were expected to reproduce for the good of the city-state. Danae is representative of the parthenos, the ideal maiden girl of ancient Greece (Langdon). Thus Acrisius commits a terrible wickedness by locking up his daughter, keeping her away from suitors. Perseus is doing justice to the idea of the parthenos by going on his quest. As Richard Caldwell explains, Perseus "kills the female monster Medusa and then marries the Ethiopian princess Andromeda, whom he finds and rescues in exactly the same situation his mother Danae had been in at the beginning of the myth; each woman was loved by her paternal uncle and had been placed by her father in a situation inaccessible to all suitors" (65). Marriage was an intensely important aspect of the Greek social atmosphere. For girls, marriage became almost the point of living. "Greeks of the Archaic period, indeed, so equated marriage and death that the same vessel…served both for the wedding bath and for decorating the graves of those who died unwed, providing the deceased, as it were, with the accoutrements of the marriage that was not realized in the present life" (*Foreign* 84). It is interesting to point out that some historians feel the very earliest Greek societies included a great deal of female equality. Many scholars argue that women possessed a large role in the guidance of the smallest Greek communities. "According to [Joseph] Campbell, the story of Perseus's slaying of the Medusa marks the overthrow of that earlier mythology and culture and the relegation of the 'female principle' to a secondary position" (Meaney 26). Thus this myth sets the tone for the rest of the Greek civilization's history by reducing women to a level just above slave. The capture by Perseus of the eye of the Graiae, the imprisonment of Danae, and Medusa's death stare all symbolize the fact that "woman is denied the power of observation…her different view will become no view at all" (Meaney 32). Despite this contention, Cassiopeia is still immortalized in the heavens, which suggests that women were not reduced in stature, but merely given a different role in society. The Perseus story illustrates this role.

The Perseus story also explains the importance of maintaining social order. Although he is a member of Greek royalty and is of divine blood, Perseus is often seen as a peasant hero because his weapon of choice, a sickle, is a peasant weapon. "It is not the short straight sword we would expect, but has a curved blade, sharpened on the inside. The harpe is the characteristic weapon of Perseus, and much has been made of it. Robert Graves…associates the sword with the sickle of the moon and Perseus with lunar aspects" (Wilk 28) Wilk also says that several aspects of the myth, including the odd birth of Pegasus and Chrysaor from the neck of Medusa, the demand of a gift of a horse by Polydectes, the golden shower of Zeus, and the fact that there are three Gorgons instead of just one can all be attributed to earlier astronomy—science shaped the myth (142). But these details are in essence the icing on a cake that is a lesson in social structure. Perseus is seen as a hero because he overcomes the problems that arise from the follies of evil kings. In this sense, "the Gorgon head…became a vehicle for rectifying past injustices and restoring a fair and equitable social balance; once in the hands of Perseus it became a positive force" (*Masks* 90). Despite being royalty, "Perseus…is both the deindividualized ritual performer of one type of social order and the ego-oriented tyrant of another" (*Foreign* 79). This idea that Perseus stops society from devolving into chaos is significant, because at the time that the Perseus story is supposed to have taken place, Greece was finally coming into its own, from a cultural standpoint. "That the Perseus-Gorgon myth is about the establishment of a new kind of order…is incontrovertible…The story of his slaying the monster is like many others wherein the defeated is represented by a mask that becomes the signal for the opening of a new and radically different era" (*Foreign* 80). Medusa's head becomes a symbol of Greek separation from earlier eastern cultures. "That the Gorgon likely was ritually associated with death and revivification is also suggested by an iconographic association between Gorgons and the wrathful Mistress figures of Asia Minor" (*Masks* 89). Greeks were historically quite wary of outsiders; Athens was infamous for its strict rules regarding citizenship. Aliens were not treated with the same social status as citizens in Greece. The Perseus myth cements this fundamental difference between Greeks and non-Greeks. A. David Napier notes that "it is important to realize that it was in the era of Peisistratus," when the Perseus legend first significantly rose in popularity, "that the division between mystic ritual and public celebration was dissolved." Napier continues, saying, "The return of the exiled Peisistratus was mirrored—even legitimated—by his support of Dionysus, the 'outsider' who embraced the common man" (*Foreign* 107). Perseus's status as a common man provided a perfect parallel. Oftentimes, city-states worshiped a mythological idea of their own founder, creating a mythology to make that founder more than just a common man. Perseus, then, serves this role for Greece as a whole. "What is important is that, in achieving cultural identity, [the Greeks] perceived themselves as having entered into some kind of symbolic exchange. They took the Gorgon head as a trophy, as the symbol of both the conquering and the assimilation of the alien; in turn they offered Perses, the son of Perseus, as the invented ancestor of the Persians. They gave, through their hero Perseus, freedom to an Ethiopian princess while taking her to become Perseus's queen—that is, queen of Mycenae, and queen, therefore, of Greece" (*Foreign* 106-107). Perseus, through his myth, establishes the importance of social order.

The mythological story of Perseus and its subsequent astronomical associations include manifestations of the fears and values of the ancient Greek culture. It is the culture that surrounds the storytellers and the star watchers which has the greatest impact on the nature of both the mythology and the astronomy of any civilization. As Lawrence Hatab puts it, myth is another way of saying culture (21). While the constellations as well as the legends of Greek mythology appear to be "larger than life," they are in reality no larger than the mortal men who shaped them.

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Parametric Study Of a Nd: Yag Laser Beam Interaction with Graphite

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ABSTRACT

Graphite is an important material in a number of specialized industrial applications due to its high thermal conductivity and resistance to thermal shock. Common applications include use as an electrode in electro discharge machining and as a mold material in metal casting. These applications often include fine details that are difficult to achieve with rotary tool machining techniques. Ablation with an Nd:YAG laser marking system permits greater detail in the machined pattern. The beam behavior and resultant mark are determined by four key operating parameters: lamp current, pulse frequency, marking speed and pattern repetition. Experiments were conducted to determine the effect of each parameter on the rate of material removal and resulting mark quality. Scanning Electron Microscopy (SEM) was employed to characterize the mark quality. Results were analyzed to determine the most efficient parameter without degrading the quality of the mark. Reducing the marking speed had the most profound effect on the material removal rate.

INTRODUCTION

Laser applications in material processing are becoming ever more common. Increased processing speed, low operating cost, and greater capabilities make laser ablation a viable alternative to traditional mechanical machining technology. This study analysed the impact of a number of operating parameters on graphite, an important material in several manufacturing methods.

One of the most notable applications of graphite is as an electrode for Electro Discharge Machining (EDM). EDM is a highly precise method of machining numerous materials. An electrode is placed close to the material surface with a dielectric liquid filling the void between the two. A current is passed through the electrode to create a controlled pattern of arcs that erode the material. The electrodes used can vary both in size and material. Often, a graphite electrode is machined so that it is a negative image of the desired pattern. Graphite is also used as a mold material for metal casting and rubber molding. High thermal conductivity and resistance to thermal stresses make it an ideal choice.

In both cases, the pattern is often limited by the size of the rotary tools available. This issue is especially troublesome when attempting to cut inside corners. The non contact nature of laser ablation eliminates these concerns.

The tests conducted fell into two categories. First, the depth of focus for the beam was determined to ensure that further testing would take place with adequate fluency. For a given set of optics there is a focal length that will maximize the beam fluency. Unfortunately, as material is removed the focal length changes. Optimally the worktable can be raised to compensate for the removed material, but this is not always possible. Alternately, a depth of focus where the laser energy is sufficient to ablate material can be determined. As long as the depth does not exceed the depth of focus, marking is possible.

The second class of tests was designed to determine the impact of the key operating parameters lamp current, marking speed, pulse frequency, and pass count on the efficiency of material removal. The selection of a parameter set involves a number of tradeoffs between time, cost, and quality. By developing relationships between parameter choice and result, it will be easier to choose the best configuration to complete a job.

EQUIPMENT

Testing was conducted using a pulsed 100W Nd:YAG laser marking system. This system consisted of the laser, interchangeable focusing lenses, and a set of computer controlled mirrors used to direct beam across workpiece. The system is mounted in a machine base with three axis workbench. This bench is equipped with a two dimensional digital readout system displaying table position. This system allows the user to measure small, precise adjustments made in the sample location before, during, or after marking.

A proprietary software suite called FobaGraf was used to define beam path. Using a simple programming language, the software gives the operator complete control over a number of important laser parameters including lamp current, marking speed, pulse frequency, as well as the number of passes that should be taken over the pattern. The software allows simple paths to be programmed. For more elaborate patterns, a tool is included to import CAD or other vector artwork files. Patterns used in these tests were all created in AutoCAD and imported.

PROCEDURE

Depth of Focus

To determine the depth of focus an apparatus was designed to allow the focal length to be systematically adjusted. The apparatus consisted of an angled bar attached to the work table. A strip of painted steel was clamped to this bar. The laser scribed a short line on the metal strip and the entire table was then translated so that the next mark would be at a different focal length. Figure 1 shows this arrangement. The apparatus was designed so that each 1mm of table movement was equivalent to a 100μm change in focal length. After marking, the strip was sectioned and examined using scanning electron microscopy. Images of the lines were obtained. Using Photoshop, the width of each line was determined. When measuring this width, both ablated metal and any disruption of the paint were included because at greater focal lengths the only mark appears on the paint.

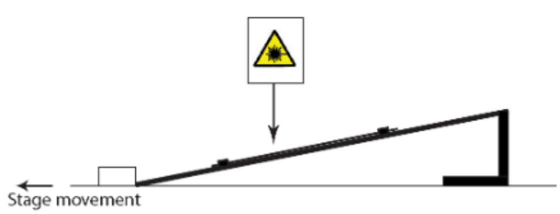


Figure 1: Focus Testing Apparatus

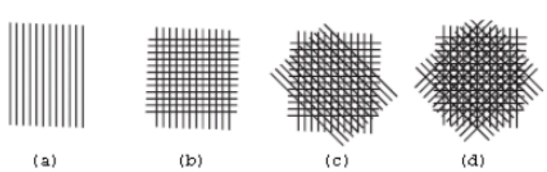


Figure 2: Hatch Patterns

Material Removal

A series of patterns were developed to test the effect of laser parameters on the efficiency of material removal. The patterns consisted of roughly 30 2mm squares. Each square was assigned a different parameter set based on the variable in interest. These values were chosen to provide a representative picture of the laser's capabilities. The focal length was chosen so that the entire depth of the square fell within the depth of focus for the system. To minimize any adverse effects associated with temperature rise in the sample material, the laser was paused briefly between squares and the squares were marked in a non-sequential pattern so that adjacent squares were never marked consecutively.

After the sample was ablated, the depth of each square was determined with the aid of a Mitutoyo digital indicator. This experimental routine was repeated on several metals to provide comparison to engineering materials traditionally processed with lasers.

Surface Finish

When the desired pattern requires the ablation of a 2D area, the area must be hatched with a series of lines to fill the area. The marking software provides a range of options to generate this hatching pattern. The most important parameters are the spacing of the hatch lines and the orientation of one or more planes. The ideal spacing between lines is the laser spot diameter. This spacing was used in conjunction with the four hatch patterns shown in Figure 2 to generate a range of surface finishes.

RESULTS AND ANALYSIS

Depth of Focus

Figure 3 The line width obtained is proportional to the laser spot size and therefore indicative of how well the beam is focused [1]. In the region close to the focal length of the optics, a smaller spot size indicates a well focused beam. The experimental line widths obtained are shown in Figure 3. Most researchers consider any beam width within $\sqrt{2}$ of the beam width at the focal point to be within an acceptable depth of focus [2] [3].The average line width for the roughly flat region at the bottom of the figure is 212μm. Based on this figure, it was determined that any focal length that produced a line smaller than 300 μm falls within the depth of focus. This includes all lines with measured focal length of 125.5mm to 131.6mm. Based on this knowledge, markings up to 6mm in depth could be created without noticeable loss of power. The user would focus the material to 125.5mm to maximize the depth possible.

Material Removal

Figure 4 is a comparison of material removal rates for a range of materials. These relationships can be used as a guide to appropriately scale the results presented below for other materials.

Lamp Current: The laser energy is supplied by a high pressure krypton flash lamp. The light from this lamp is used to excite electrons in the Nd:YAG rod to start the chain reaction resulting in a laser pulse. The output power of the laser is directly proportional to the output power of the lamp, which is in turn controlled by the current supplied to the lamp. The output power should increase with the square of the current. This relationship is shown in Figure 5. It can also be noted that the laser did not have enough power to remove material until the current reached 17A and then follows a roughly parabolic pattern. The lamp current is independent of time, making high current processing most time efficient. It was also observed, however, that since more energy is imparted in the same amount of time, there is a greater likelihood that thermal damage will occur. Although observed less frequently on graphite, these thermal impacts must factor into the decision on what current to use.

Pulse Spacing is based on the relationship between pulse spacing and marking speed. The two parameters must be balanced so that each spot overlaps the previous to form a solid line. This result is obtained with any combination of the parameters such that the translation of the beam between pulses is less than the spot size. With increased overlap, more material is removed per unit distance covered. Although this increases the amount of material removed per pass, the time it takes to complete the pass is increased. In addition, pulses produced at high frequency contain less energy than lower frequency pulses. Figure 6 shows the results these trials. Based solely on the measured depth, it appears that the rate of material removal can be maximized by choosing a low marking speed. In reality, however, there is a strong time dependence in the data. It takes significantly longer to complete a marking at 5mm/s than at higher speeds. To correct for this inherent time dependence, the data was normalized to a marking speed of 200mm/s, the rate used for all

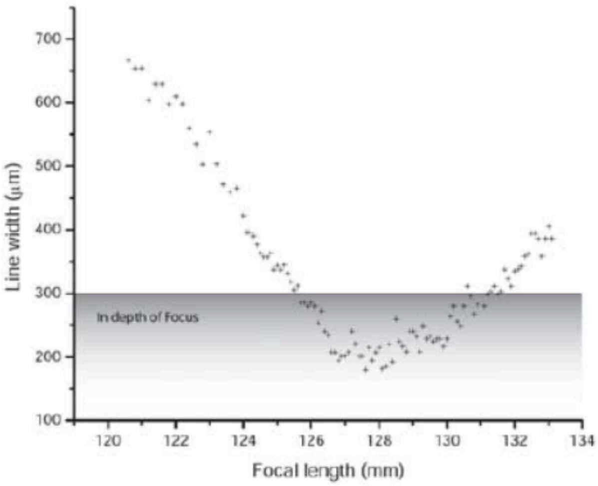


Figure 3: Measured Line Widths

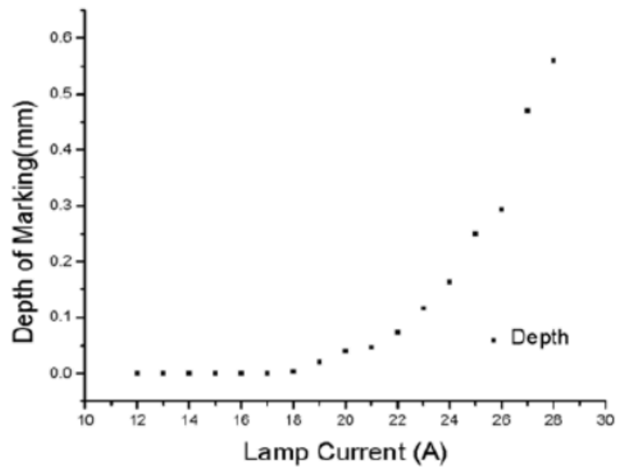


Figure 5: Increase in lamp current causes nonlinear increase in marking depth.

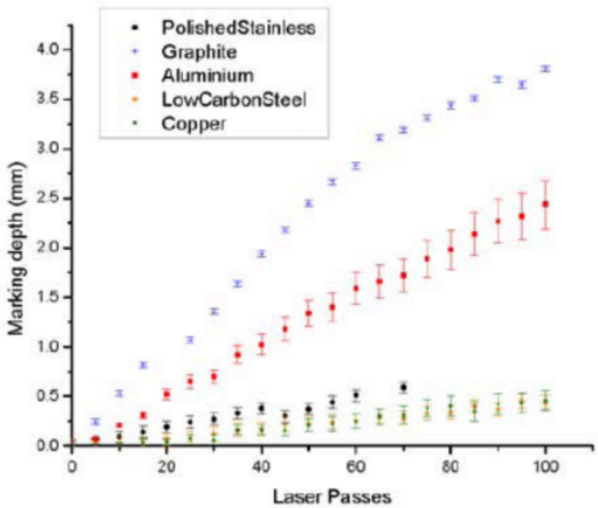
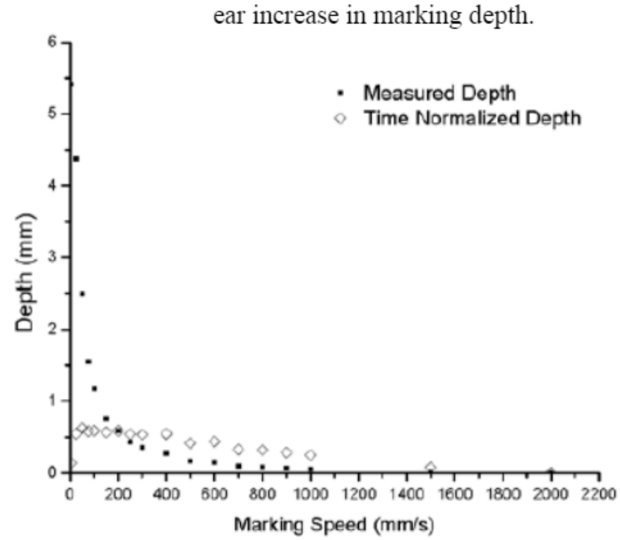


Figure 4



other tests. It then becomes clear that there is little change in actual material removable rate as the marking speed is changed and the normalized depth of approximately .6mm corresponds well to that obtained with a 28A lamp current.

<u>Pass Repetition:</u> Once configured, the control system can be instructed to repeat the marking as many times as are needed to achieve the required depth or until the depth of marking is greater than the depth of focus. The pattern was run twice. The first set of data used hatch

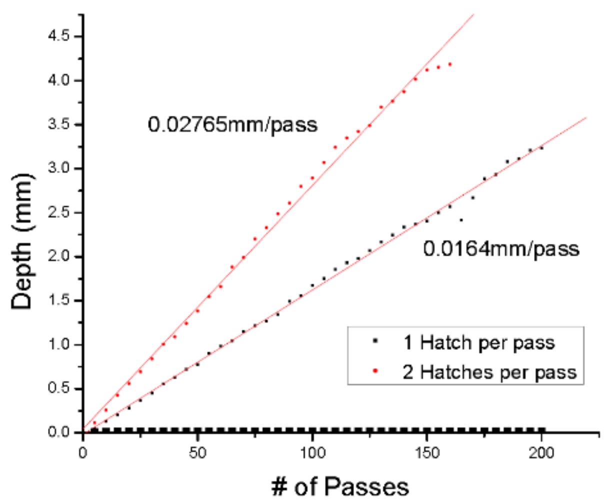


Figure 6: Increasing pass repetition increases the depth of marking.

pattern in Figure 2a. The second test was run with the pattern in Figure 2b. Figure 7 shows this data, accompanied by the slope of the respective tests. It is expected that since twice the number of passes are taken in the second configuration, the material would be removed at twice the rate. Contrary to this hypothesis, the experimental results showed an increase of only 70% in the rate of material removal. It is seen that increasing the number of passes increases depth, but there is again an introduced time factor in the data. The actual rate of material removal is derived from the slope of this line, and is therefore constant. One advantage of the of the linear nature of this parameter is that the final depth can easily be controlled by increasing or decreasing the number of passes.

Surface Finish

A WYCO non-contact optical surface profilometer was used to characterize the surface of the four hatching regions. Due to the low reflectivity of graphite, a thin layer of gold was sputtered onto the surface. Figure 7 shows the surface profile generated by the hatch patterns as well as an SEM image of one region in Figure 8 . Table I contains quantitative data from this analysis.

The complexity of the marking increases in proportion to the number of hatch orientations. As more layers are added, especially at non right angles, the pattern takes longer to process due to the extra beam translations required. In addition, the likelihood that the hatch pattern will not align perfectly with the edge of the marching increases with the number of layers marked. This can be seen in Figure 9.

Based on these criteria, it is desirable to choose the hatch style with the fewest layers to mark the pattern. Examination of Figure 7 shows that if only one orientation of hatching is used, the resulting pattern has a series of high ridges and deep valleys. By adding perpendicular hatching, these high ridges are knocked down. This is enforced by the largest Rq (root mean squared roughness) value for the single hatch. The least rough of the patterns was the area marked with the two layer cross hatch, making this a an ideal choice for hatching.

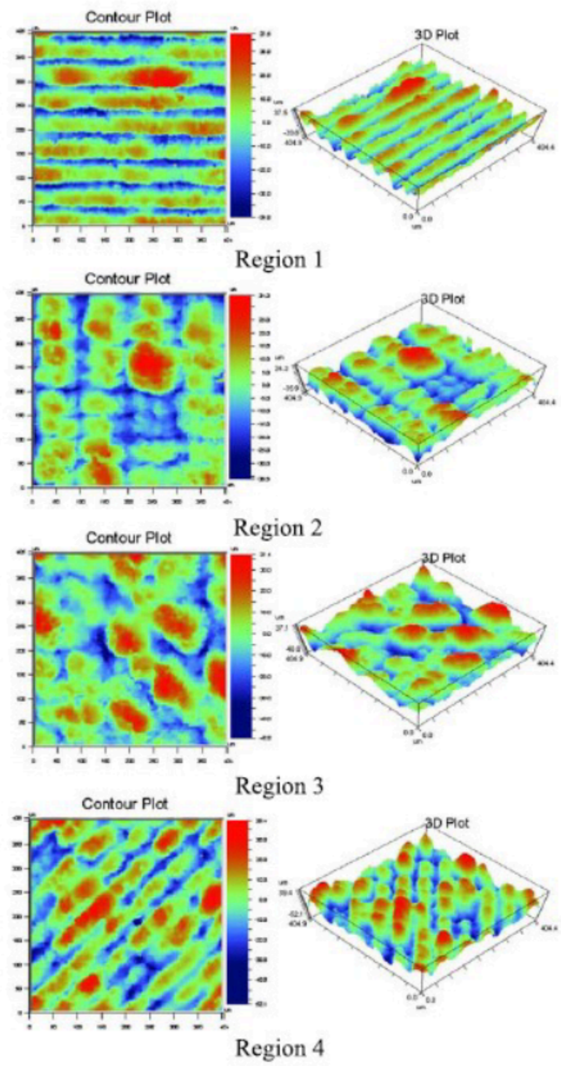


Figure 7: Images or four hatch regions examined.

CONCLUSIONS

While increasing capability in design is an important motivation in choosing laser ablation as a method of machining graphite, the driving factor is always cost. The key controllable variable in the cost of machining is the time it takes to run the pattern. Of the three key operating parameters, current is the only parameter that allows for time independent increase in the material removal rate. Increasing pattern repetition or reducing marking speed also increased the depth of the markings, but also led to longer processing times. By adding additional orientations to the hatch pattern the ridges and valleys generated can be broken up, but the effect is most pronounced with two hatch directions offset by 90°.

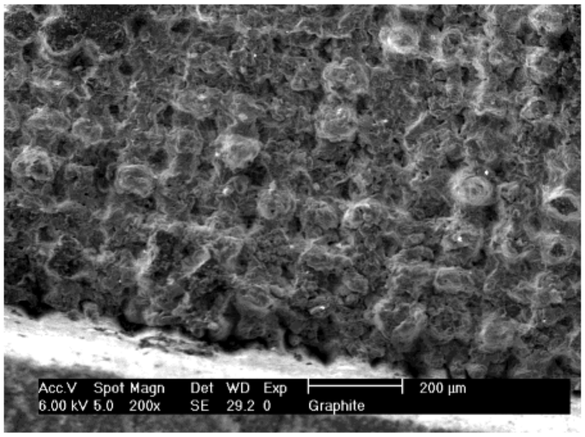


Figure 8: Graphite marked with hatch pattern in Figure 2 (b)

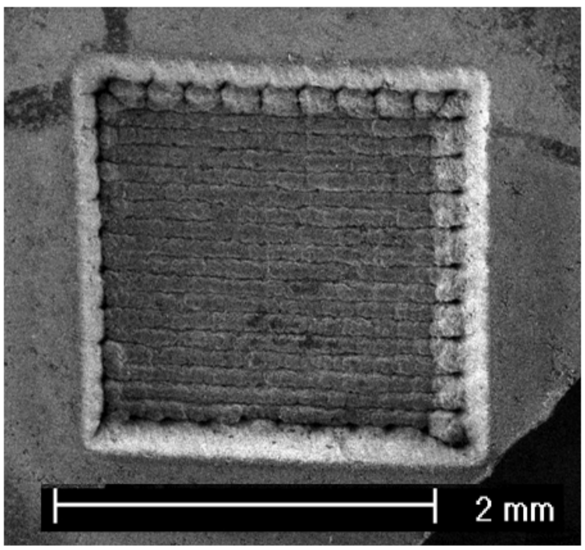


Figure 9: Hatch pattern did not remove material along upper and right borders of object.

Sample	Rq (µm)	Rz (µm)
1 (Pattern a)	13.08	75.27
2 (Pattern b)	10.36	63.96
3 (Pattern c)	12.06	74.92
4 (Pattern c)	12.1	76.47

Table I: Rq (Root Mean Square Roughness) and Rz (Maximum peak to valley separation) of the four hatch patterns analyzed.

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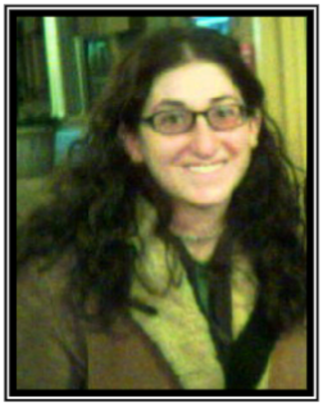
Individualized Behavioral and Image Analysis of Response Time, Accuracy, and Social Cognitive Load During Social Judgments in Adolescents



-Brooke Schepp-

Brooke Schepp is a senior at Case Western Reserve University where she is a triple major in Biology, Psychology, and Cognitive Science. She also has a minor in Chemistry. Aside from being active in the research community, Brooke has also been very active on campus. She acted as a director for the CWRU Film Society for two years and she is an active member of the Case Taekowndo club. She has also acted as an SI (supplementary instructor) for COGS 102: Introduction to Cognitive Neuroscience and is a member of Psi Chi, the national honor society in psychology. After graduating in May, Brooke will spend two months backpacking through Europe and then plans to attend graduate school in the fall.

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ABSTRACT

Functional magnetic resonance imaging (fMRI) has become an invaluable tool in understanding the relationship between brain and behavior. This technique has become particularly important in the study of human social cognition. The current study focuses on the social cognitive judgment skills of late adolescents (ages 18 -21), and seeks to investigate four specific aims. These aims include the following: 1) To characterize the relationship of accuracy of responses and reaction time while making social judgments; 2) To describe the relationship between response accuracy and social cognitive load; 3) To identify the relationship between questions of increasing social cognitive demand and reaction time; and 4) to identify the interaction between response time, accuracy, and increasing social cognitive load. A secondary aim of this study is to complete an individualized functional imaging analysis taking into consideration each participants' accuracy and reaction time. This analysis will provide further insight into the brain-behavior relationship in human social cognitive function. Behavioral and imaging results of the present study will be reviewed.

INTRODUCTION

Social cognitive skills, such as the detection of sarcasm, the expression of humility, and the sharing of the conversational burden, are vital for successful social interactions with peers, especially during adolescence when individuals are faced with increasingly complex social interaction (Turksra 2000). The use of functional imaging technology has allowed investigators to examine the neural mechanisms responsible for social cognitive skills (Saxe 2006). Some of the brain regions identified as important for social cognitive behaviors include the superior temporal gyrus, anterior cingulate, fusiform gyrus, parahippocampal gyrus, and inferior parietal lobe (Ciccia, et al. 2006).

The present study investigates the behavioral effects of reaction time, accuracy, and level of social cognitive load on the functional imaging methodology currently used by Ciccia (2006) to study brain activation patterns during social cognitive judgments in adolescents. A secondary aim of this study focused on using the results of the behavioral analysis to customize the functional imaging analysis. Tailoring the functional imaging analysis to each participant's social decision reaction time will allow for a more valid investigation of the imaging results.

METHODS

Participants

All participants in this study met the following inclusion criteria: 1) No history of neurological disease or disorder (including acquired brain injury); 2) No history of learning or reading disability or gifted states; 3) No history of claustrophobia; and 4) No metal in their body (e.g., pacemaker wiring). The participants ranged in age from 18 to 21 years, with a mean age of 19 years, and included four male and four female participants.

A total of fourteen participants completed the study; however, only data from eight of these participants could be analyzed. Four participants could not complete the study because of illness at the time of the scan, one participant was removed from data analysis because of clinical findings discovered when the file was reviewed by a Radiologist, and another participant was removed from data analysis because of equipment malfunction during the functional imaging protocol.

Imaging Tasks and Behavioral Procedure

Tasks:

Participants were shown videos of different social conversation interactions that occurred between adolescent actors (Turkstra, 2000). Conversations focused on topics that were identified by adolescents as appropriate and likely to be brought up in normal conversation. These included topics such as after school activities, classroom performance, friendships, and dating. Social conversational skills that were depicted in these interactions included detection of sarcasm, expression of humility, and sharing conversational burden.

After watching each video, participants were asked to make a series of social judgments of increasing difficulty based on the interactions just viewed (Figure 1). The first social judgment, requiring minimal social cognitive demand, was, "Is X interested?" (X referring to a specific actor in the video clip). The participants were then shown the same clip a second time and asked, 'Does X get it [the meaning]?' This question required a moderate amount of cognitive demand. After a final showing of the video clip, the participants were asked the high-level cognitive demand question, 'Does Y think that X gets it [the meaning]?' where Y refers to the second actor in the conversation.

Figure 1: This figure shows video clips from the paradigm with the three questions used in the study. In this video, the female character is trying to elicit sympathy and compassion from the male character by telling him that her dog died this morning. The male character is not paying much attention to her or her story. The video was shown three times to each participant, with one question being presented in this order after each video clip.

A total of three blocks, with five video vignettes in each, were shown to the participants. Each of these videos was shown three times within a block. Each video and each block was followed by a period of rest of either four or six seconds where the participant was presented with a blank screen. There was a sixteen second break following the last question in each block. Figure 2 depicts the paradigm design for each block, including rests. Each video clip, including decision making time, equaled a total of ten seconds. Following each clip, the participants had a three second window to give a response, although it was possible for them to give a response even after the next video had started. Each block took a total of 3:06 minutes.

Procedure:

Informed consent was obtained and a practice session was completed before the participants entered the scanner. The practice session lasted one hour and consisted of reviewing social rules and practicing the video paradigm on a computer. The review of social rules included questions such as: "What makes a good/ bad communication partner? What makes a conversation go well? How do you know?"

The functional imaging protocol took place at the Cleveland Clinic Foundation and was completed within 48 hours of the practice session. Prior to beginning the functional imaging protocol, the video para-

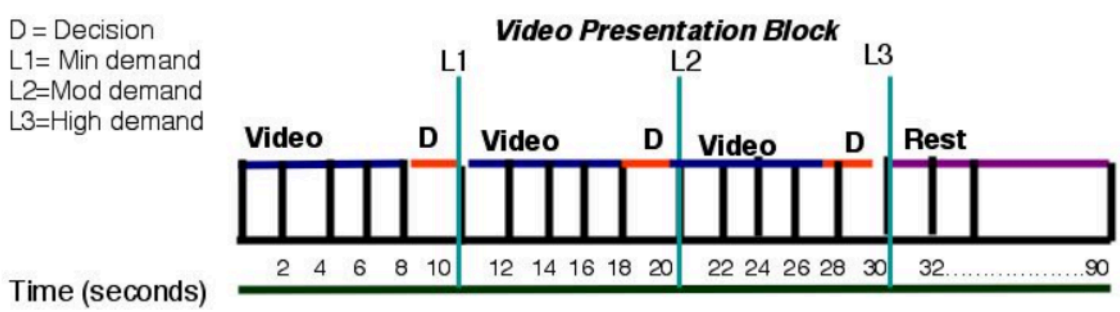


Figure 2: Video Presentation Block, an example of the video design shown in this experiment. The participants were shown a video example of a common social conversation. After viewing the video, the participants were asked to make a series of social judgments, which were presented in an order of increasing difficulty. The participants saw each video clip three times, each time followed by a different question. There were five individual video clips in each block.

digm was practiced outside the scanner for a second time and the imaging technician answered any questions the participant's may have had about the scanner.

Aside from watching the video paradigm, the participants were also required to make behavioral responses according to their social judgments. Participant responses were collected using 5DT virtual reality data gloves. The gloves were placed over the hands of the participants, who would then make minimal hand movements to register their response. The participants were instructed to move their left hand to indicate "no" and their right hand to indicate "yes". The participants were given the opportunity to practice this response pattern, with the gloves on, prior to completing the video protocol in the scanner and again between video block presentations.

To ensure the comfort and safety of participants during the fMRI protocol, time in the scanner was limited to one hour and a foam pad was placed under each persons' head and knees. Additionally, participants were in constant contact with the researchers via an audio system that allowed researchers to hear the participants at all times. Participants were also given a "panic button" which would alert the research staff of any type of emergency. Each participant removed any metal from their bodies (e.g. earrings) prior to entering the scanning area.

Data and Image Acquisition

Data for this study was acquired using a 3T Siemens Allegra MRI scanner located at the Cleveland Clinic Foundation. The video paradigm was presented via back-projection and a mirror was fixed to the head-coil in the scanner and was in line with the participants' field of vision. The trigger for the video paradigm was coordinated with data acquisition from the fMRI scanner through MATLABã software. The behavioral responses captured using the 5DT virtual reality gloves were coded and were reviewed by an independent member of the study at a later date.

The imaging protocol consisted of the following: Anatomic scans consisted of 3D Whole brain T1:T1 -weighted inversion recovery turboflash (MPRAGE), 120 axial slices, thickness 1.2mm, Field-of-view (FOV) 256mm x 256mm , TI/TE/TR =1900/1.71/900ms, flip angle (FA) 80º, matrix 256 x 128, receiver bandwidth (BW) = 32kHz. Imaging for the fMRI activation study: 101 EPI volumes of 32 interleaved axial slices were acquired using a prospective motion-controlled, gradient recalled echo, echoplanar acquisition (Thesen et al., 2000) with TE/TR/flip=39ms/2s/90º, matrix=64x64, 256mm x 256mm FOV; BW = 125 kHz.

Imaging Data Analysis

Imaging data were processed and analyzed using Statistical Parametric Mapping (SPM5) software developed by the Wellcome Department of Imaging Neuroscience at the University College in London (http://www.fil.ion.ucl.ac.uk/spm/software/spm5). Preprocessing analysis of the data included: slice timing correction, realignment and unwarping, co-registration, normalization to the MNI T1 template (Montreal Neurological Institute), and smoothing with a 6 mm isotropic Gaussian kernel. These preprocessing steps allow SPM to combine the functional and structural imaging data into a single image for analysis. Realigning takes all of the separate imaging files and puts them into the software program in the order in which they were taken. This process was completed for the structural imaging scans and the functional imaging scans separately. Another preprocessing step, spatial normalization, takes into account the normal variation in individuals head size. The images were then smoothed to accommodate differences in individual brain structures and prospective motion correction was used as a primary method to deal with participant movement within the scanner. Following this, grey-matter segmented and smoothed MPRAGE images were combined with mean EPI images averaged across subjects to create a single union image. Individual subject data were analyzed in a fixed effects model with the Canonical HRF as basis functions. The six realignment parameters (3 rotations and 3translations) were included as repressors. SPM identifies functionally activated coordinates and indicates cluster size. Significant cluster size was defined as 54 voxels or greater. The completion of these tasks allowed for a clear overlay of the functional imaging data over the structural data and the identification of activation in pre-specified regions of interest (Frackowiak, Friston, Frith, Dolan, Price, Zeki, Ashburner, & Penny, 2004).

Standardized Group Imaging Analysis

Ciccia and colleagues (2006) previous analysis of the group data looked at the brain activation patterns that persisted across all study participants. To analyze the group data, a single reaction time decision point was identified each social judgment. The ten second time point was selected because a preliminary inspection of the behavioral data indicated many participants registered their decisions at the ten-second mark. This data was then looked at in two ways: as a group image (where the 10 second decision points for all of the participants were averaged together), or as individuals (each individual participant's activation using the same ten second marker as the decision point). Activation patterns where then compared according to question difficulty to discover which brain areas are activated by different levels of social judgments (Ciccia, 2006).

Individual Imaging Analysis

The image analysis for the present study considered each participants brain activation patterns rather than grouped results as discussed by Ciccia and colleagues (2006). Although many of the decision points fell on the ten second mark, the actual variability in reaction times varied from in from 7.85 seconds to 12.05 seconds. The exact second of response was pinpointed from the behavioral glove response data. This temporal information was used to individualize the functional imaging analysis in SPM. These scans were then divided up into groups that correlated to question difficulty (i.e. all of the response times for the firsts question, 'Is X interested?' were put into one group, etc.) and these groups were compared against each other in order to find to activation effects that were specific to each question set. In other words, by subtracting out the activations caused by the simplest question (Is X interested?) from the activations caused by the most difficult question (Does Y think that X gets the meaning?) the areas of the brain used solely for the most difficult question become highlighted. The subtraction method allows researchers to see what brain areas are activated as adolescents are faced with more challenging social judgments.

The results from the customized individual analysis completed for this study were then compared to the individual analysis previously conducted by Ciccia and colleagues (2006) that used a standardized 10 second decision time.

Behavioral Data Analysis

The behavioral data analysis focused on the responses that the participants made while answering the social questions during the functional imaging protocol. The laser gloves allowed the computer software (MATLAB) to register each response as yes or no and to register the reaction time for each decision. Data for reaction time and yes/no responses were organized by subject, question type, block order, and accuracy in a way that was appropriate for statistical analysis. Researchers in the lab identified correct and incorrect answers based on agreed upon criteria. Each participant's responses were then coded as correct or incorrect and the data was entered into SPSSã statistical software (http://www.spss.com) to complete an analysis of the specific aims of this study which included: 1) the relationship of reaction time to response accuracy (correct and incorrect answers); 2) the relationship between reaction time and question type; 3) the relationship between accuracy and question type; 3)and the interactions between accuracy, question type, and reaction time.

RESULTS

Behavioral Data

It was first determined that all participants completed all three blocks. Only one participant failed to make social judgments (i.e. not giving a response when prompted with the questions) during the paradigm. This same participant also remained undecided on four responses (by moving both hands in response to a question, thus answering both yes and no). Since these six responses all occurred for the same participant and during the same block, results from that block were discarded. It was also noted that for the last participant response in each of the blocks was not collected by MATLAB. This left only fourteen question responses per block for analysis, resulting in a loss of twenty four responses of questions of type three. The information gleaned from the behavioral response data (reaction time, accuracy, and question type) were run though SPSS in order to determine main effects and the interaction effects these three variables.

Accuracy vs. Reaction Time vs. Question Type

The relationships between these three variables are very complex. These relationships are illustrated in Figure 3. The first thing to note is that the reaction time of all question one responses (both correct and incorrect) have a faster reaction time then questions of type two and type three. The response times of questions of type three appear slightly faster then those of type two. The second thing to note is that the reaction times of the correct responses are faster then the reaction times for incorrect responses. It is also of interest to note that there seems to be more variation in reaction times for incorrect answers as compared to correct answers.

A relationship that is not represented in this figure but what was clear in the data is that there were more correct responses then incorrect responses. Overall, there were 243 correct answers, 87 incorrect answers, and six undecided or null responses. Of these, questions of type one had the most correct responses, followed by questions of type two followed by questions of type three. Questions of type two had the most incorrect responses, with the number of incorrect responses

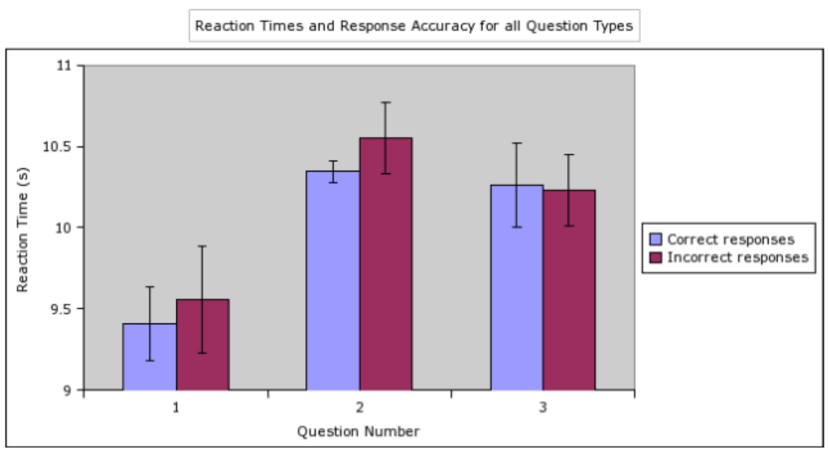


Figure 3: This figure shows the interaction between response time and accuracy across all question blocks. This data demonstrates that Questions of type one had a much faster reaction time then questions of type two and type three. Questions of type two had the slowest response followed closely by questions of type three. This data also shows that correct answers have a faster reaction time then incorrect answers.

being roughly the same for questions of type one and questions of type three. A MANOVA was run with all of the variables to determine the relationships between reaction time, accuracy, and question type. This test determined that there was a significant main effect for the relationship between these three variables ($p = .000$ for all variables). Additional post-hoc testing and testing of between subject effects revealed additional information about the nature of these relationships, which are discussed further in this section.

Accuracy vs. Question Type

Overall, there were 92 correct responses, 24 incorrect responses, and four null or undecided responses for questions of type one. There were 81 correct, 38 incorrect, and one null or undecided response for questions of type two, and there were 70 correct, 25 incorrect, and one null or undecided response for question three (not including the 24 missing question three responses). This data can be seen in Figure 4. Overall, it does not appear that question type has any real effect on accuracy. Questions of type one had the most correct responses, followed by questions of type two and then types three. Using SPSS, it was determined that that the relationship between accuracy and question type is not statistically significant. This was true across all question types (Tukey HSD P = .897, .897, and 1.000; LSD p = .661, .661, and 1.000 for Q1 Q2, Q3, and Q1, Q2, Q3 respectively).

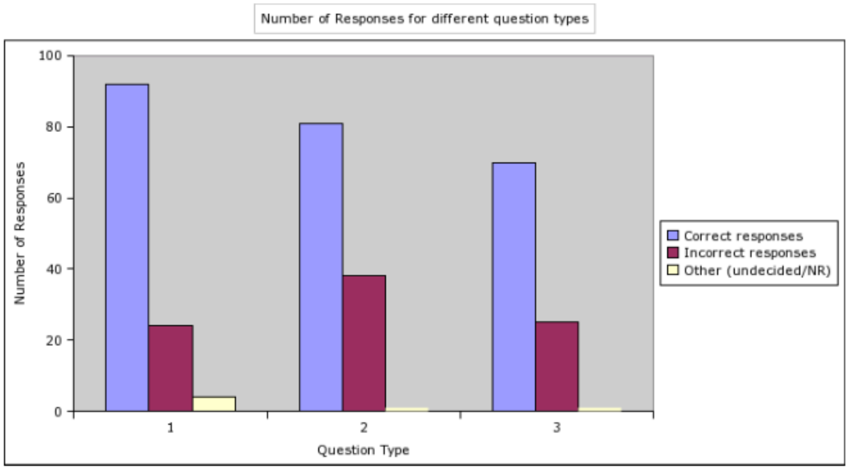


Figure 4: This figure shows the number of correct and incorrect responses per question type. These results demonstrate that correct responses were much more prevalent then incorrect responses. "Other" responses include answers where the participants or replied with both 'yes' and 'no' responses. The data indicated that questions that required a low social cognitive load had more correct answers then questions which required a higher social cognitive load. This data is skewed by the missing data in two of the question sets.

Question Type vs. Response Time

The mean reaction time for each block was 10 seconds (10.05s ± 0.6s, 10.07s ± 0.57s, and 10.03s ± 0.67s for blocks 1, 2, and 3 respectively) and the overall response time was 10.05s ± 0.60s. This gives credence to the decision to use 10 seconds as an average response time for the analysis previously conducted by Ciccia and colleagues (2006). It is also important to note that the response times did not change over the course of the study. Having the same response time over all three blocks indicates that the participants were not getting faster or slower as the study progressed. Separating the responses by question type, it becomes clear that reaction time varies by changes in social cognitive load. Specifically, the data indicates that question type ones had a faster reaction time then either questions two or three. As Figure 5 indicates, this difference in reaction time seems to be restricted to question one versus question types two and three, and there does not appear to be any difference in reaction time between questions of type two and type three.

The mean reaction time for question type ones over all blocks is 9.54s ± 0.71s. This is appreciably lower then the mean reactions times of questions of type two and three (10.32s ± 0.29s and 10.36s ± 0.18s respectively) and could mean that the actual time of response for questions of type one could be located in the scan before the one that was looked at in the group data. The differences in reaction times can be clearly seen in Figure 6. It is also of note in this figure that the first questions asked in each block have a slower reaction time then any other question type one in the study. In fact, the reaction time of this first question is often higher then those of the other question types.

The relationship between question type and response time was determined in post-hoc testing. It was determined that there was a significant difference ($p = .000$) for Question 1 as compared to questions two and questions three. No significant difference was found between response times for questions two and three (Tukey HSD $P = .951$, LSD $P = .766$).

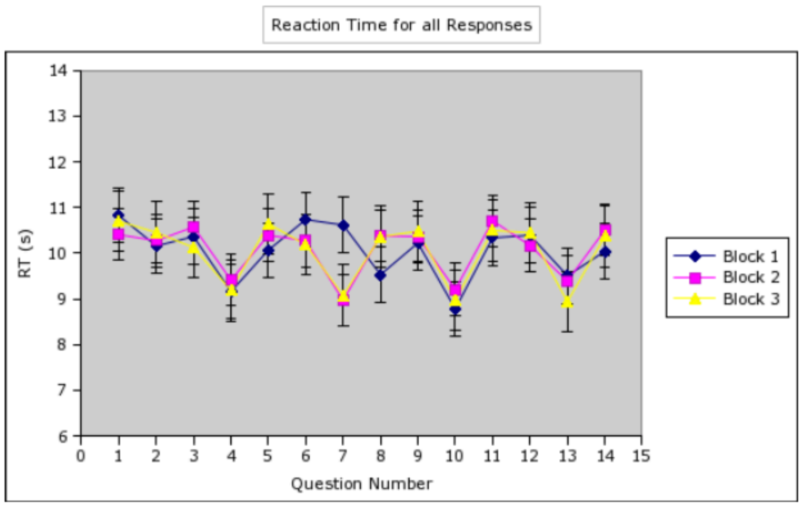


Figure 5: This graph shows the average reaction times for questions during the three blocks. This data indicates that, on average, questions of type one had a faster reaction time. This was true across all blocks. This data also indicates that questions of type two and type three similar reaction times.

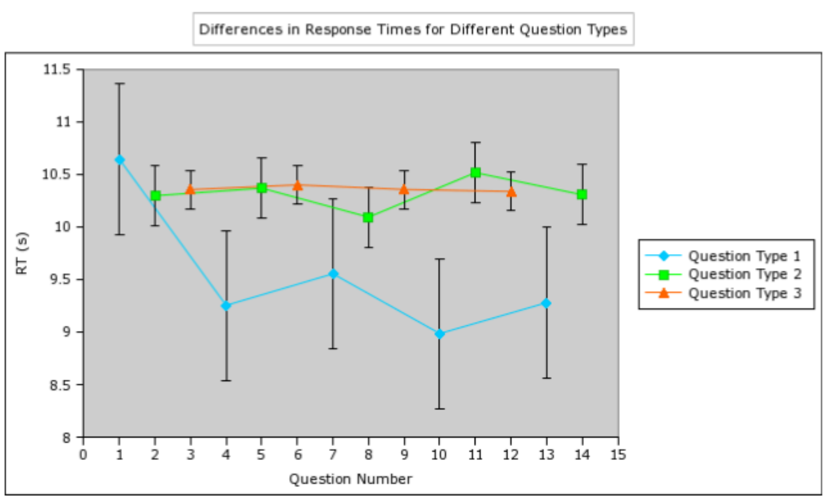


Figure 6: This figure shows the response times for different question types. Questions of type one (representing questions requiring the lowest social cognitive load) had the fastest response time of any of the questions. Questions of type two and of type three (representing moderate and high social cognitive load) have about the same reaction times.

Response Time vs. Accuracy

Further analysis of the behavioral glove response data showed that participants made correct social judgments faster then they made incorrect social judgments. The mean reaction time for correct answers was 9.97s ± 0.23s while the mean reaction time for incorrect answers was10.23s ± 0.47s. These results are shown in figure 7.

This finding demonstrates that the response time of the participant to the social stimuli was highly dependant on the participants' accuracy on the task. A t-test showed there to be a significant difference in reaction time for correct and incorrect answers, t(286), P = .000; t(87), P = .000. It is also of interest to note the differences in the variances between the correct and incorrect reaction times. While correct responses took roughly the same time across all blocks, incorrect response times had a greater variation. This is particularly clear in Figure 8. These figures are also important in that they illustrate that participants were neither getting more accurate or inaccurate as the study progressed.

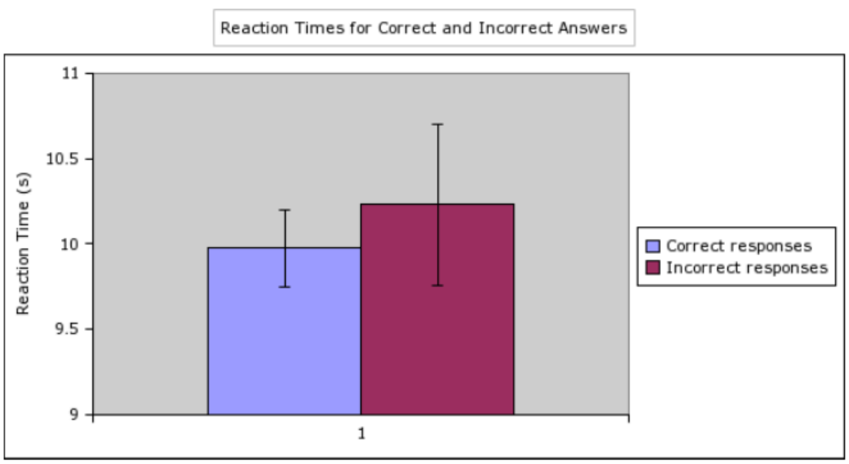
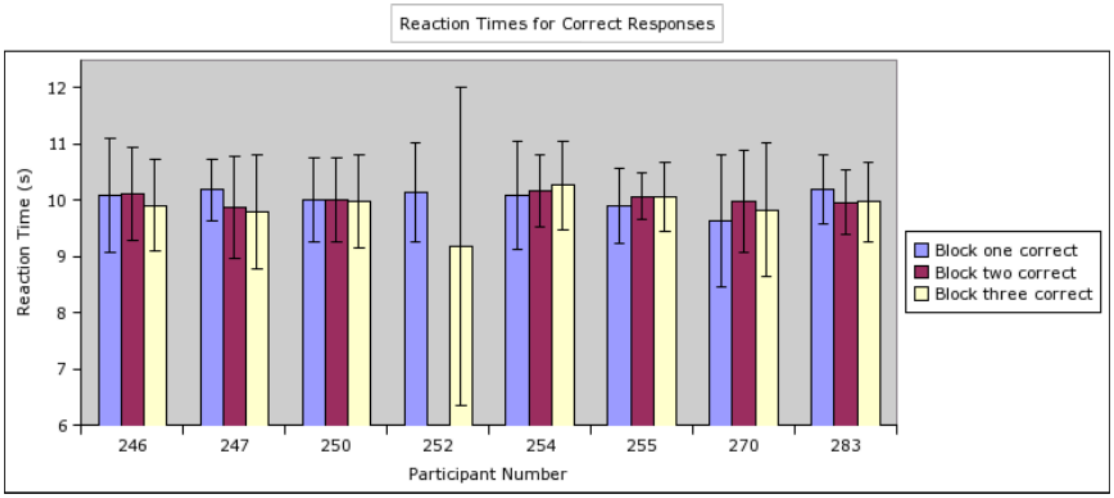


Figure 7: This figure shows the average reaction times for correct and incorrect answers. The data indicates that correct answers had a faster reaction time then the incorrect answers. The data also indicates that incorrect answers had a wider variation of responses as compared to the correct responses.

Another interesting item to note about the relationship between response time and accuracy is how it changes over time. Originally, correct and incorrect answers have about the same reaction time, with correct responses (m = 10.09s ± 0.43s) taking slightly longer then incorrect answers (m = 10.00s ± 0.68s). During the second block, the response times for correct and incorrect answers become nearly identical, with the response times of the incorrect answers (m = 10.11s ± 0.56s) increasing and the response times of the correct answers (m = 10.09s ± 0.53s) decreasing slightly. By the third block, the reaction times of the incorrect answers (m = 10.23s ± 0.41s) has continued to increase while the reaction times of the correct answers (m = 9.84s ± 0.63s) has decreased. The end result is that the response times of incorrect answers increase over time, while the reaction times of correct answers decrease over time. This data can be seen in figure 9.

Imaging Analysis

The imaging analysis previously completed by Ciccia and colleagues (2006) identified the following areas to have significant areas of activation during tasks of high social cognitive demand (represented by questions of type three) as compared to tasks of minimal so-



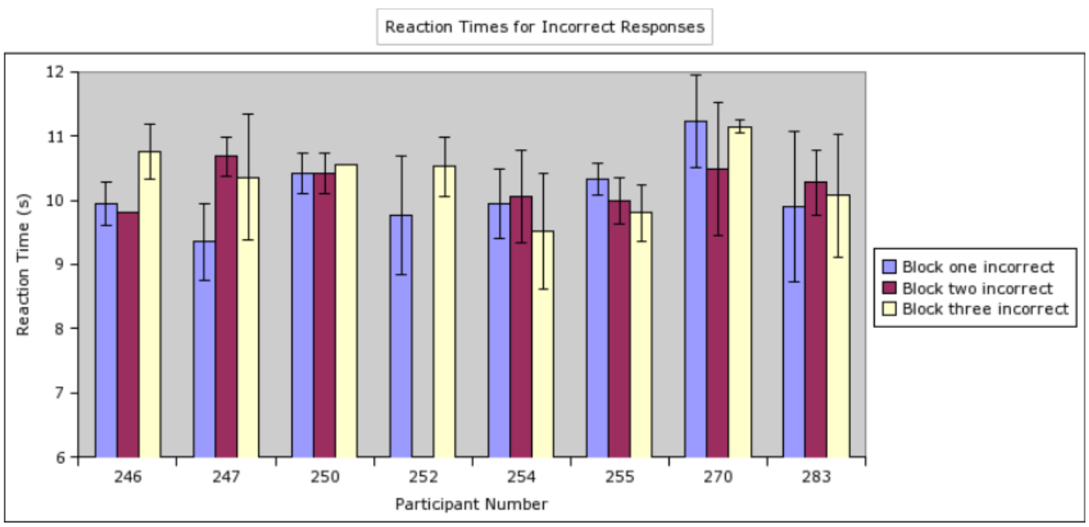


Figure 8: a) This section of the figure shows the reaction times for correct answers for all participants across all blocks. b) This section of the figure shows the reaction times for incorrect reaction times for all participants across all blocks. These figures demonstrate that correct answers had a faster reaction time then incorrect answers. The data also indicates that there was greater variability of reaction times for incorrect answers then there was for correct answers.

cial cognitive demand (represented by questions of type one) included: the left superior temporal gyrus (BA 22), the left anterior cingulated gyrus (BA 32), the left fusiform gyrus (BA 37), the right parahippocampal gyrus (BA 19), and the right inferior parietal lobule (BA 40). These results can be found in Table 1 and Figure 10.

Significant areas of activation during tasks of high social cognitive demand (represented by questions of type three) as compared to tasks of moderate cognitive demands (represented by questions of type two) include the following a priori regions: the left fusiform gyrus (BA 37), the left inferior parietal lobule (BA 40), the right anterior cingulated gyrus (BA 24), and the right inferior parietal lobule (BA 40). These results can be seen in Table 2 and Figure 11.

There were no significant areas of activation identified for the tasks of moderate social cognitive demand (represented by the questions of type two) as compared to tasks of a minimal cognitive demand (represented by questions of type one).

The imaging analysis completed for the present study yielded different results from those found by Ciccia and colleagues (2006). In the analysis for the present study, the scans representing the actual decision times were compiled and input into the SPM software. The most accurate and most inaccurate participants data were analyzed. These analyses demonstrate that there is a difference in activation between these two methodologies. Figure 12 demonstrates these drastic differences between the two methodologies.

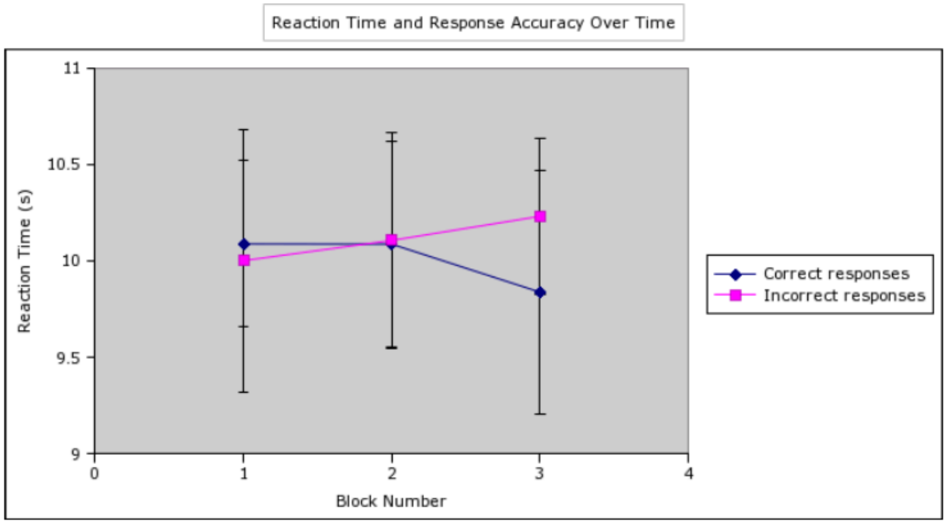


Figure 9: This figure demonstrates the reaction times of correct and incorrect answers over time (across blocks). In the first block, correct answers took slightly longer to answer then incorrect answers. In the middle block, correct answers take about the same amount of time, with incorrect answers taking slightly longer to answer. By the third block, the incorrect answers take an appreciably longer amount of time to answers then correct answers. Overall, there is an inverse relationship between reaction time and accuracy and as time goes on it takes less time for participants to answer questions correctly.

The top left image in the figure shows the results the most accurate participant, from the individual analysis using exact reaction times. The top right image shows the results for the most accurate participant from the Ciccia et al (2006) analysis. The bottom left image shows the results for the most inaccurate participant from the individual analysis using exact reaction times. The bottom right image shows the results for the most inaccurate participant from Ciccia's (2006) data. It is clear from these four images that it makes a difference whether or not the exact reaction time points are used in an imaging analysis.

Region	BA	X	Y	Z	Cluster size	T value
L superior temporal gyrus	22	-50	4	7	638	13.48
M dorsal anterior cingulate	32	-4	36	20	1282	11.19
R superior temporal gyrus/sulcus	21	**44**	-2	-10	618	9.84
R parahippocampal gyrus	19	20	-45	-6	922	8.18
L fusiform gyrus	37	-32	-45	-11	775	7.76
R inferior parietal lobule	40	61	-26	29	308	6.42

Table 1: This table shows the areas of activation during tasks of high cognitive demand as compared to tasks of low cognitive

Region	BA	X	Y	Z	Cluster size	T-value
R inferior parietal lobule	40	61	-31	37	550	14.45
R ventral anterior cingulate	24	4	34	13	3073	14.06
L fusiform gyrus	37	-30	-45	-16	6246	12.87
R insula	13	34	-14	-1	542	12.02
L superior parietal lobule	7	-30	-48	54	365	7.54

Table 2: This graph shows the areas of activation during a task of high cognitive demand as compared to tasks of low cognitive demand. These images were made using the traditional 10s time point as an average decision time.

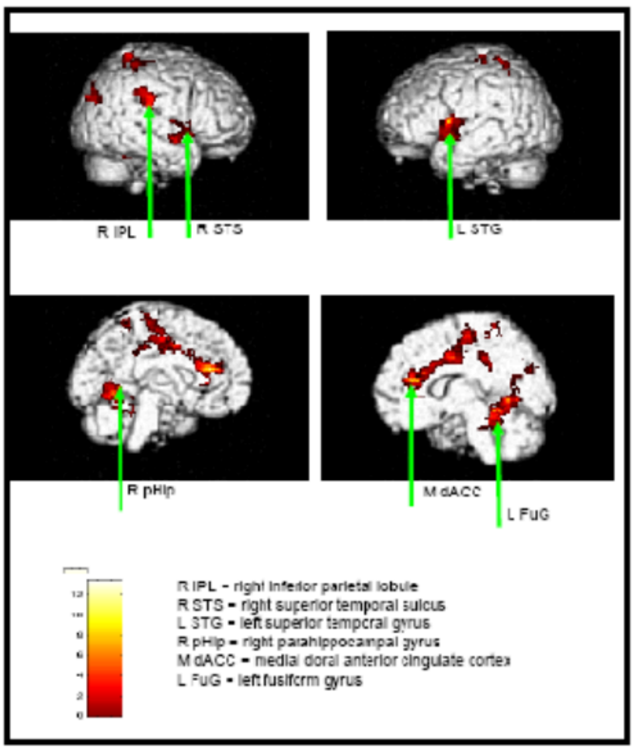


Figure 10: This figure shows the areas of activation during tasks of high social cognitive demand as compared to tasks of moderate cognitive demand. These images were m

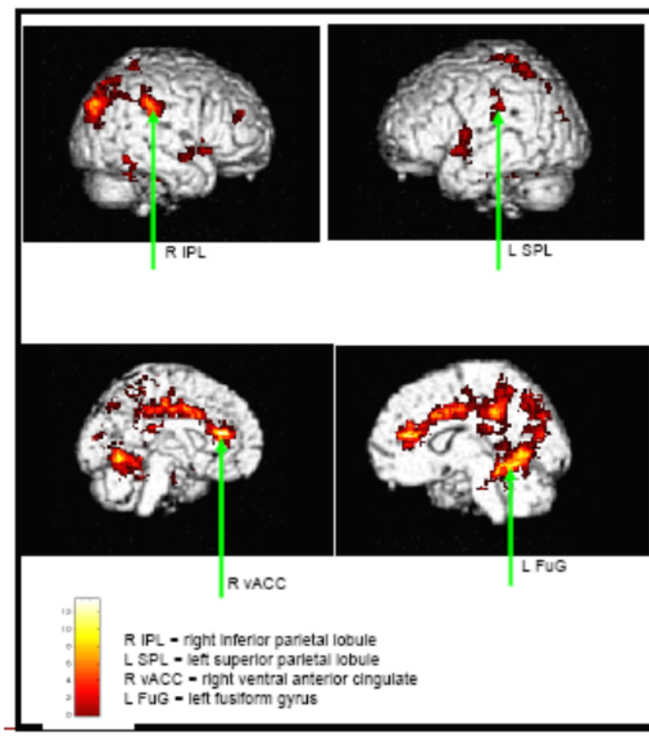


Figure 11: This graph shows the areas of activation during a task of high cognitive demand as compared to tasks of low cognitive demand. These images were made using the traditional 10s time point as an average decision time.

DISCUSSION

The results of this study supported the relationship between accuracy, reaction time and question type when analyzing behavioral responses of adolescents when making social decisions. Specifically, the analysis reveled that participants made correct social judgments faster then they made incorrect social judgments and that reaction time was significantly related to question type, with questions with lower social cognitive load taking less time than more difficult social cognitive questions.

The results of this study showed that the number of correct answers decreased over time. These decreasing correct answers could represent the effects of increasing the social cognitive load. This result may have been impacted by the loss of answers from questions of type three when question number 15 from each block from the study was lost because of a software problem with MATLAB. The results also could have been affected by missing data from all stimuli in block two from one the participants. Additionally, results may have also been skewed slightly by the difference in the number of correct versus incorrect answers. There were significantly more correct responses then there were incorrect responses. However, this result is not surprising, as this study employed a test of normal social interaction, and called upon a sample of participants with no history of social problems or deficits.

Correct responses took significantly less time to answer then incorrect responses. It is very interesting that note only did participants take a longer to answer incorrectly, but their increase in amount of time does not appear to have improved their accuracy. There are many reasons why this could have occurred. The first is that the participants either knew the answer, or they did not, right away. When they knew the answer immediately, they did not have to put any thought into generating their response. When they did not know the answer, they may have had to slowly work through the question and wound up getting it wrong regardless of their increasing in time spent considering their response. Inaccurate answers could have also taken longer because the partici-

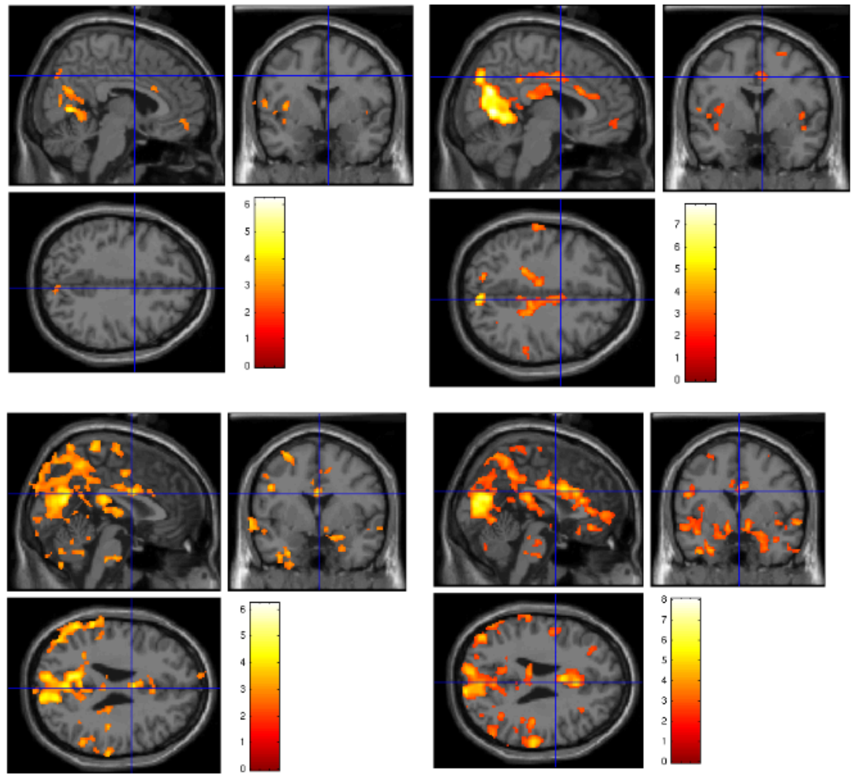


Figure 12: This figure shows the differences between the two methodologies. The images on the left were created using the exact reaction time methodology. The images on the right are those created by the original 10s method used by Ciccia and colleagues (2006). The images represent the same decisions, and should be the same if the two methods were equal. The top two images come from the most accurate participant and the bottom two images come from the most inaccurate participant.

pants were thinking about them harder. Additional analysis of the situation could lead them to both longer reaction times and incorrect answers.

Theoretically, it is not surprising that questions of type one took the shortest amount of time to answer. However, it was a surprising finding that questions of type two and type three took almost the same amount of time. The third question was hypothesized to be the most difficult in the set and required the greatest amount of cognitive load, therefore would take the longest amount of time. This was not the case. It could be that the third question was not as difficult as the researchers intended. It could also be that eventually all difficult social questions reach an asymptote and wind up taking similar amounts of time. Even though questions of type one took the least amount of time, the first question of type one in each block took the same amount of time, or longer, then questions of type two or three. It has been hypothesized that, due to the time break in-between the blocks and the practice sessions that occur between them, restarting the block means that the participants need to readjust their internal timing to the paradigm, and that results in participants taking longer to answer the first question in each block. By the second question in each block, the participants seem to readjust to making the required social judgments.

The results of the behavioral data analysis were used to analyze the functional imaging data of the most accurate and the most innacurate participants. This portion of the analysis was conducted to identify differences in patterns of brain activation when individual response patterns were used as the foundation of the analysis as opposed to a group mean reaction time. As can be seen in the data, the use of individualized response times in the imaging analysis did alter the results of the functional imaging analysis. It should be noted at this point that for the original analysis, summing the data may have produced the best results. Choosing this average decision was helpful in that is allowed researchers to average the data and to look at it as a whole, instead of looking through each individual participant. This current research demonstrates that although a standard response time can be applied as a framework to conduct the functional imaging analysis, it does not take into account the individual variation in performance, both in terms of accuracy and response time, which is important to ensure valid interpretation of imaging findings. Taken together, these results have important implications for modifications in the functional imaging paradigm used to study social cognition using Ciccia's (2006) current protocol.

It is important to note that there were many limitations in this study, including missing data for twenty-four responses to questions of type three due to problems with the response gloves. Because of the missing data, any trends that might have existed specifically for questions of type three may have been skewed. In addition to this, the responses of a singular participant to question block two had to be removed from the study due to inappropriate responses (i.e. failing to answer a question or answering both 'yes' and 'no'). Although the information with the VR gloves was accurate enough for this study, the next study will change to a button response box. The researchers believe that this will be more successful within this study for a number of reasons. The first is that a button-pressing response paradigm is more natural, and might require less training and concentration then just moving a finger. The use of the response box could lead to fewer instances of undecided (answering both yes and no) answers. The response box also allows for more rigorous accounting of reaction time. Unlike the present system, where a movement of a gloved hand causes a waveform pattern which indicates the moment of response on a continuous time scale, the button system would log the exact time of the response (reducing the time required to go to the waveform image and manually note the response time). This would give a more accurate account of response time, and, since the system is disabled after a participant responds to a question set, there would be fewer instances of undecided responses.

Although the methodology of the original study worked well, this research demonstrates that more specificity is needed when it comes to social cognitive functional imaging analysis. The next step in this study will be to do a full analysis of the imaging data taking individual reaction time and accuracy into account and using the individual analysis to conduct a group data analysis. In addition, the improvements in the current paradigm will allow for application of this paradigm with an adolescent clinical population that has know social cognitive deficits, such as Autism or Asperger's syndrome.

The results of the present study will help shape continued work in this lab in the areas of methodological improvement, in-depth comparative behavioral and imaging data analysis, consideration of developmental effects on neural activation, and applications to a variety of clinical populations with social cognitive deficits. Specifically, the lab hopes to due an individual-based functional imaging analysis on the effects of accuracy on individuals region of interest activation. The lab also plans to study inactivation in the group data as well as in the individual data.

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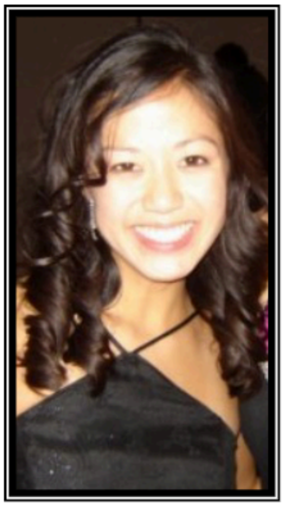
Effects of Neural Lesions on a Context -Dependent Molluscan Muscle



-Amanda Hong-

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ABSTRACT

Many muscles may have more than one function depending on their mechanical context. For example, in the human arm, the brachioradialis contributes to pronation when the hand is supinated, and to supination when the hand is pronated. We are interested in studying muscles whose function is context dependent, that is, the direction of the force or torque that they generate changes sign as a function of their mechanical context. Previous modeling studies have suggested that the posterior part of the I1/I3/jaw complex in the mollusk *Aplysia californica* can change the direction of the forces it exerts as a function of its mechanical context. In particular, when the grasper (radula/odontophore) is behind the I1/I3/jaw complex, the muscle acts to push the grasper towards the esophagus, i.e., to retract it. A kinetic model and *in vivo* studies of the I1/I3/jaw complex using magnetic resonance imaging suggest that when the grasper is anterior to the back part (posterior) of the I1/I3/jaw complex, which occurs during the strong protractions of biting, the posterior part of the muscle can act to protract the grasper.

To test this hypothesis, we performed unilateral lesions on individual branches of the nerve that innervates the I1/I3/jaw complex, buccal nerve 2 (BN2). Its three branches (referred to as "a", "b", and "c") have been shown to have different effects on the I1/I3/jaw complex. Specifically, shocking branches "a" and "c" causes the anterior part of the I1/I3/jaw complex to contract, whereas shocking branch "b" causes the posterior part of the I1/I3/jaw complex to contract. We therefore hypothesized that uni-

lateral lesions of branch "b" (BN2-b) would cause deficits of the peak protraction of biting. Results show that unilateral lesions of the other two branches of BN2 cause no significant changes in biting behavior, whereas unilateral lesions of BN2-b cause a specific deficit in biting. At the peak of normal biting protractions, the radula remains protracted for an extended period of time. After the BN2-b unilateral lesion, the radula begins to retract significantly faster on the side ipsilateral to the lesion. These results support the hypothesis because they suggest that forces that would ordinarily be expressed in the posterior part of the I1/I3/jaw complex are necessary for the radula to remain protracted for an extended period of time near the peak of biting. These studies will help to clarify the neural control of context dependent muscles in many other animals.

INTRODUCTION

In order to understand the relationship between neural signals and their corresponding movements and behavioral responses, the muscular function involved must also be understood. However, the role of muscular function may be complicated, because a muscle may exhibit more than one function depending on its mechanical context. A previous study using cadaver specimens and computer modeling showed that the moment arms of muscles crossing the elbow are substantially dependent upon forearm and elbow position. In particular, these experimental results showed that elbow flexion moment arms increase substantially with elbow flexion and are greatly affected by the pronation/supination angle (Murray *et al.* 1995). In other words, the brachioradialis muscle in the human arm contributes to moving the forearm in opposite directions, depending on the initial position of the arm. Another study quantified the effects of postural variation in the biomechanics of six human shoulder muscles. Results showed that the mechanical function of each muscle varied substantially with arm posture. This variation was dependent upon one or more angles defining arm posture within the respective frame of reference (Buneo *et al.* 1997). Another study used similar methods to characterize the mechanical actions of the hindlimb muscles of the cat. Results showed that the cat flexor and extensor muscles generated large extra-sagittal torques that were joint angle dependent with regards to both magnitude and sign (Lawrence and Nichols, 1999a, Lawrence and Nichols, 1999b).

These studies suggest that the mechanical function of a muscle may be context-dependent in that the direction of the force or torque they generate changes sign as a function of their mechanical context. Previous research has explored the functional relationships between neural control and muscular behavior through methods such as biomechanical modeling. However, in many species, the complexity of the organism's nervous system makes in depth studies impractical. The marine mollusk *Aplysia Californica* is an ideal organism for experimental study due to its relatively simple nervous system. Commonly known as the sea slug, *Aplysia* has large identifiable neurons and an easily accessible buccal mass, or feeding apparatus. Feeding behaviors are also easily elicited by tactile stimulation with seaweed laver, facilitating observation of biting behaviors.

Aplysia feeding structures lack a hard skeletal system, and instead function through forces provided by muscle and cartilage. Due to the many degrees of freedom and great flexibility in movement, comprehension of biomechanical properties is necessary in understanding the neural control. Previous kinematic and kinetic modeling studies have suggested that the posterior part of the I1/I3/jaw complex in *Aplysia californica* can act in a context dependent manner through its ability to change the direction of the forces it exerts as a function of its mechanical context.

The jaw musculature's context-dependent function was previously tested through a kinetic model of the buccal mass. This model tested the mechanical advantage as the radula/odontophore moved during biting behaviors (Sutton *et al.* 2004). They found that early activation of the I1/I3 muscle complex could indeed assist in moving the radula/odontophore in the anterior direction during protraction.

Magnetic resonance imaging data further supports the context-dependent hypothesis through imaging of the internal structures of the buccal mass. The temporal and spatial resolution of the experimental images enabled direct measurement of the anteroposterior lengths of the I1/I3/jaw musculature both dorsally and ventrally, and thus facilitated kinematic measurements of the muscles of the buccal mass during swallowing behaviors (Neustadter *et al*. 2002b). These studies showed that the radula/odontophore midline is anterior to only the posterior half of I1/I3 during peak protraction in biting. Therefore, only this posterior half would be capable of intensifying protraction, advocating that this posterior I1/I3 acts in a context-dependent manner.

In fact, the I1/I3 muscle complex may have context-dependent effects that intensify protraction during biting and retraction during swallowing, as shown by magnetic resonance images and I1/I3 lesions. Observations of the buccal mass have shown that the hinge muscle also aids in moving the anterior portion of the radula/odontophore into position to allow the I1/I3/jaw complex to push the radula/odontophore strongly in the posterior direction (Ye *et al.* 2006). The kinetic model shows that the function of the I1/I3 muscle can be changed by modifying the timing of I2 and I1/I3 muscle activations in relation to each other. The model showed that if activation of I3 begins during the protraction phase while I2 is still being activated and the radula/odontophore has not yet returned to rest, the radula/odontophore will then protract more strongly and for a longer period of time. This behavior was tested through implantation of extracellular electrodes in the I2 muscle and on buccal nerve 2 (Chiel *et al.*, unpublished observations).

Kinematic models suggest that the I3 muscle plays an important role in retraction during swallowing, and further suggest that if I3 is anterior to the midline of the radula/odontophore when at rest, contraction of I3 will induce movement in the posterior direction, and vice versa (Neustadter *et al.* 2002a). Previous lesion studies testing this context-dependent hypothesis included I3 cartilage lesions and bilateral BN2 lesions, comparing jaw widths, rates of ingestion and rejection, and time from peak protraction to jaw closure. The I3 cartilage lesions prevent the I1/I3 muscle complex from fully closing the lumen of the jaws without affecting the neural innervation. BN2 lesions, on the other hand, remove the neural innervation of the I1/I3 muscles, effectively paralyzing the I1/I3 muscles with the exception of passive forces. The effects of these lesions reduced the intensity of both the protraction and retraction phases during biting and rejection, respectively (Chiel *et al.*, unpublished observations).

Other lesion studies explored the effects of bilateral lesions of each of the branches of buccal nerve 2. It was known that buccal nerve 2 innervates the I1/I3 muscle complex; however, the effects of a single-branch lesion on I1/I3 and radula/odontophore behavior were unknown. This study showed that a lesion on buccal nerve 2 branch b resulted in a reduction in biting protraction for animals performing large amplitude bites (McManus, unpublished observations).

This experiment focuses on the effects of a unilateral lesion on buccal nerve branch b, and thus tests the hypothesis that the posterior I1/I3 exerts a protractive force during biting.

Figure 1. Schematic view of camera set-up apparatus and camera angles.

MATERIALS AND METHODS

Observations and Lesion studies

Aplysia Californica (Marinus, Long Beach, California) marine mollusks ranging from 200 to 500 grams in weight were randomly chosen after being aroused to food, and demonstrating vigorous biting responses. In order to obtain behavior identical to that in natural conditions, observations were performed in fresh artificial seawater produced from Instant Ocean sea salt mix. The tanks were maintained at temperatures between 14 to 17 degrees Celsius and at a salinity level of approximately 36ppt. Bio-Bag disposable filter cartridges were used to ensure that the environment of the mollusks was kept in acceptable condition.

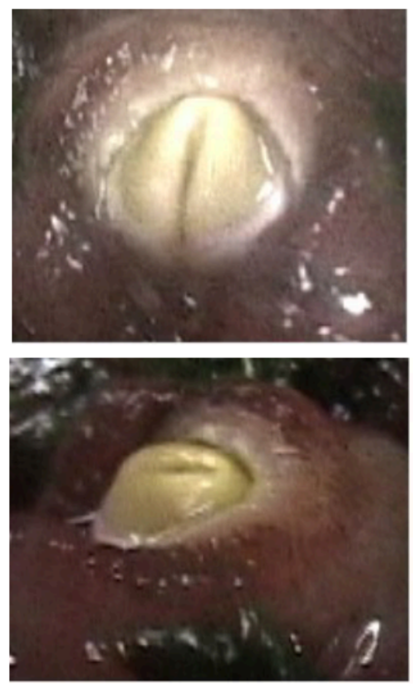

Figure 2. Views from each camera. The picture on the left shows the view from camera 1, and the picture on the right shows the view from camera 2.

The *Aplysia* specimen was then placed in a large Petri dish after obtaining its weight by difference. Pre-lesion behavior was observed through video recording using two Canon NTSC 2R60 digital video camcorders in a two-axis configuration with an algorithm for three-dimensional reconstruction video analysis (algorithm designed by Gregory Sutton and Jeff McManus; camera

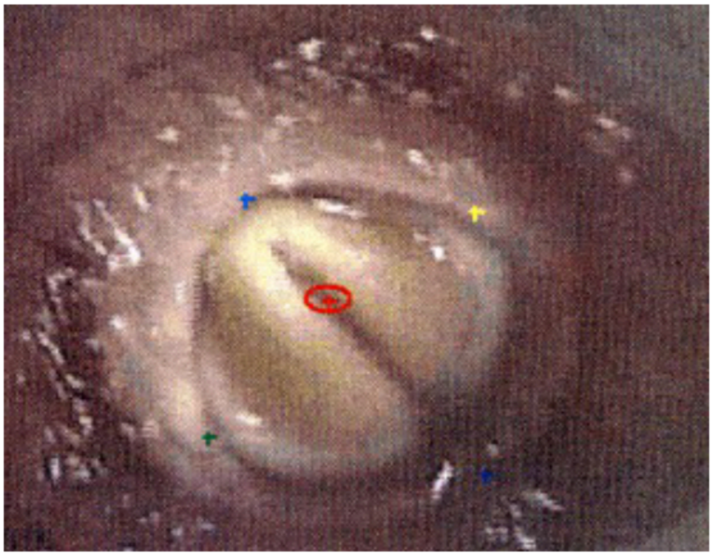

Figure 3. Frame showing the five points plotted on the jaw line and radula. A point was placed at both extremities of the jaw (blue points), as well as on both sides approximately in the middle (green and yellow points). A fifth point (red) was placed in the middle

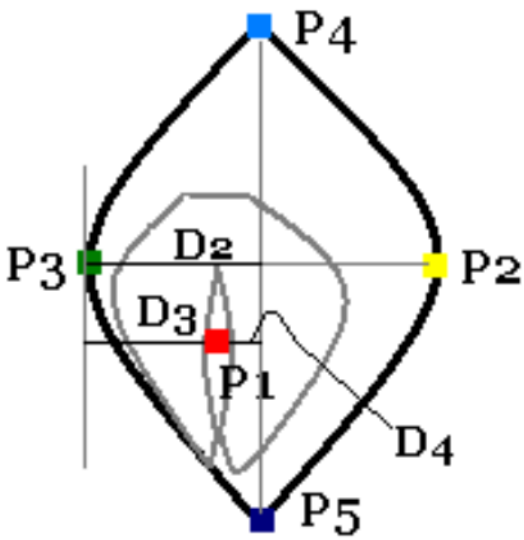

Figure 4. Drawing of radula and jaw with point and distance configurations. D2 and D3 were calculated for both sides of the jaws.

set-up designed by McManus) as shown in Figure 1. The views from each camera are shown in Figure 2.

Biting responses were induced through bilateral stimulus with seaweed laver. This method resulted in a better view of the slug's jaw and protracting radula. After obtaining sufficient footage of biting behavior, the sea slug was placed in a dissecting tray with a small amount of artificial seawater. A perimeter of Styrofoam blocks was then secured around the sea slug with dissecting pins to minimize movement. The edges of the tray beyond the Styrofoam perimeter were then packed with the ice, and the tray was placed in the freezer for approximately fifteen minutes. The Styrofoam blocks were then removed and ice was placed directly on and around the slug. The tray was returned to the freezer for approximately thirty to forty minutes until the slug appeared to be completely relaxed (i.e., anesthetized).

The slug was then pinned to the tray with dissecting pins through its tail and each anterior tentacle. A small incision approximately one centimeter in length was made along the vertical axis of the dorsal side of the specimen, starting approximately one centimeter forward from the rhinophores. This incision was then held open using four paperclips on strings tightly fastened to the edges of the dissecting tray. The buccal mass was rotated to either the left or right side, and a unilateral lesion *in vivo* of buccal nerve 2, branch "b" was performed. After returning the buccal mass to its original orientation, the incision was sutured with Ethicon K-890H 5-0 black braided silk, using a 13 mm Ethalloy™ needle.

The same procedure was followed for control experiments, except that a unilateral lesion *in vivo* of buccal nerve 2, branch "a" or "c" was performed instead. A total of three experimental and three control trials were completed, consisting of two lesions of the right buccal nerve 2-b, one lesion of the left buccal nerve 2-b, one lesion of the right buccal nerve 2-a, one lesion of the right buccal nerve 2-c, and one lesion of the left buccal nerve 2-c.

After the slug recovered from the lesion surgery (typically about two days after the surgery), and resumed normal eating behavior, post-surgery feeding responses were recorded again with digital camcorders in the two-axis configuration described above.

Once post-surgery behavior was recorded, the lesion was then checked to ensure that nerve re-growth had not occurred. The slug was anaesthetized with injections of 50% isotonic $MgCl_2$ (333 mM) solution until the slug no longer retracted from external stimulation. The buccal mass was then dissected out of the slug and examined under a microscope to ensure the lesion of the nerve branch had no regeneration. For all data reported in this paper, no regeneration was observed.

Data Analysis

The video footage was exported to iMovie, and several clips of individual bites were extracted from each pre- and post-surgery trial. Three clips from each trial were analyzed with the WinAnalyze program. Five points were plotted on each frame, starting when the radula halves touched together after peak protraction until the radula had retracted back into the mouth and was no longer clearly discernable. The five points were chosen in order to calculate several distances of interest using the three-dimensional reconstruction coordinates of WinAnalyze. The point configuration is shown in Figure 3.

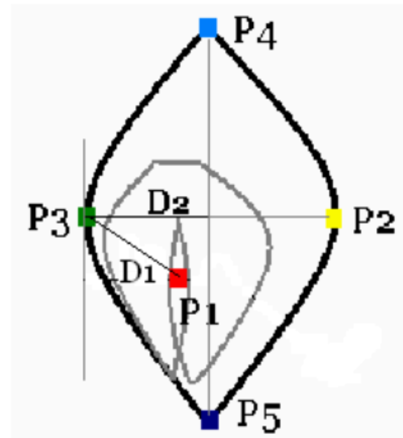

Figure 5. Drawing of radula and jaw with point and distance configuration. D1 and D2 are computed in three-dimensional space without any projection corrections for both sides of the jaw.

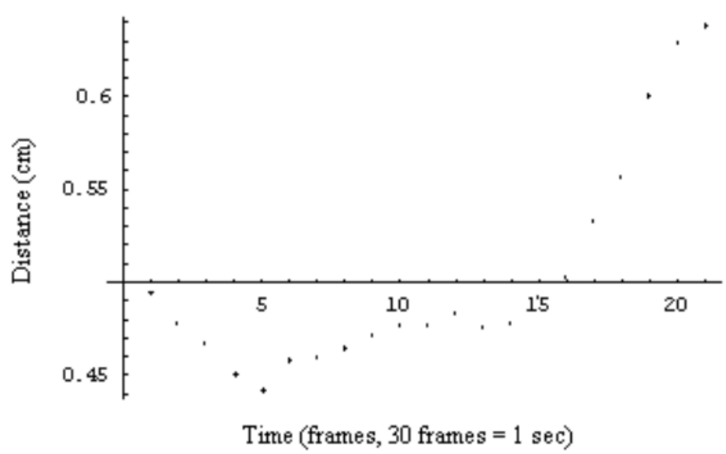

Figure 6. Real distance data from one trial of pre-lesion behavior.

The WinAnalyze three-dimensional reconstruction data was then exported and analyzed using *Mathematica* (analysis program written by Jeff McManus). Evaluation produced graphs showing the projected distance from the bisecting midline to the side of the jaw (D2), the projected distance from the radula center to a line parallel to the side of the jaw (D3), and the projected distance from the radula center to the midline (D4), or radular shift. Figure 4 shows a schematic drawing of the placement of points and the distances of interest.

As shown, P1 is a point in the middle of the radula surface (between the radula halves), P2 and P3 are on the jawline along the sides of the mouth, and P4 and P5 are on the jawline at the front and back corners of the mouth. This is a three-dimensional object resulting in a configuration of non-planar points.

Initial calculations computed the distance in three-dimensional space from the middle of the radula halves to each side of the mouth (D1), and the distance from the bisecting line across the middle of the mouth to either side (D2) as shown by Equations 1 and 2 (point-line distance formula; see Figure 5).

$$D1 = |P3 - P1| \quad (1)$$

$$D2 = |(P5 - P4) \times (P4 - P3)| / |P5 - P4| \quad (2)$$

This configuration was meant to show the faster shift of the radula and jaw closure on the lesioned side as compared to the non-lesioned side. However these distances contain many sources of confounding error due to movement up and down the z-axis (into and out of the mouth). Since the jaw and radula complex is not on a single plane, movement of the radula center (P1) up and down through the jaws can increase both distances, leading to distorted trends. Figure 6 shows a sample of this data.

This is corrected by using a cross product of two existing vectors to form a vector perpendicular to the jaw plane. The two initial vectors are constructed from P4 to P5 (V1) and from P2 to P3 (V2). The resulting vector, V3, can be used to define a plane using any other point. Equation 3 and Figure 7 illustrate these calculations.

$$V3 = V1 \times V2 \quad (3)$$

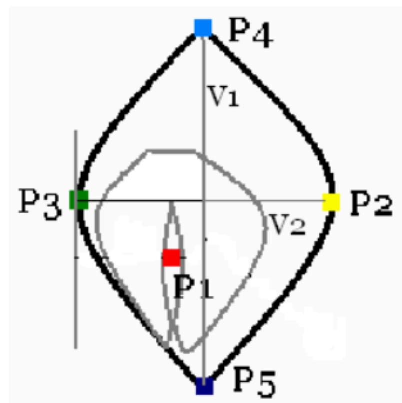

Figure 7. Drawing of radula and jaw showing vector configuration. V3 is the cross product perpendicular to the jaw plane (out of the page).

V3 is then used to find another perpendicular vector from P1 at the split of the radula halves by defining another point, P6, shown in Equation 4. Equation 5 then describes the intersection of the line through P1 and P6 with a plane perpendicular to V3 and containing P2 and P3 (the "jaw plane").

$$P6 = P1 + V3 \quad (4)$$

$$u = V3 \cdot (P3 - P1) / V3 \cdot (P6 - P1) \quad (5)$$

The intersection point, P7, between the line from P1 to

P6 and the jaw plane is then found.

$$P7 = P1 + u(P6 - P1) \quad (6)$$

The resulting distance from P3 to P7 is the projected distance of D1 (as shown in Figure 6). A sample of this data is shown in Figure 8.

Although this counteracts error due to z-axis movement, this projection does not account for error due to forward/backward movement of the radula. To counteract this new source of error, the direct distance from the radula center to a line along the side of the jaw, as shown by D3 in Figure 4, was calculated. This distance was found by defining another point, P8, to form a line parallel to V1 through P3.

$$P8 = P3 + V1 \quad (7)$$

Using the point-line distance formula, the distance from P7 to this new line was calculated, resulting in a projected distance D3 (shown schematically in Figure 4).

$$D3 = |(P8 - P3) \times (P3 - P7)| / |P8 - P3| \quad (8)$$

This projected distance shows the best approximation of the distance from the center of the radula to the side of the mouth. A sample of this data is shown in Figure 9.

This same method of calculation was used to obtain the projected distance from the midline to either side of the mouth, represented as D2 in Figure 4. These projection calculations are necessary to account for error due to z-axis and forward/backward movements of the radula that would otherwise confound and distort changes in distance.

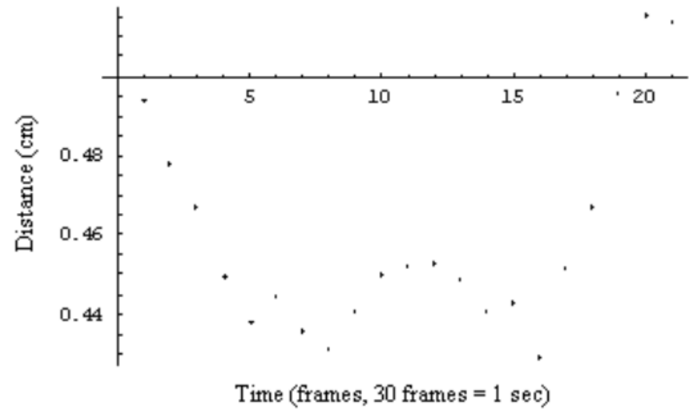

Figure 8. Projected distance D1 from one trial of pre-lesion behavior (same trial as shown in Figure 7).

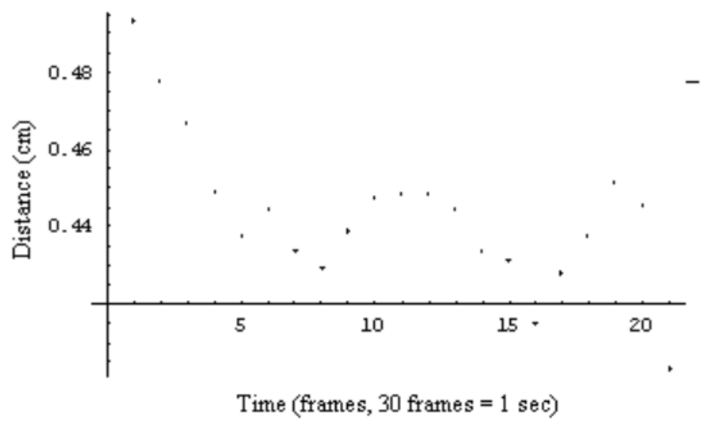

Figure 9. Projected distance data corrected for y-axis movement from one trial of pre-lesion behavior (same trial as shown in Figures 6 and 8).

The last distance of interest is the projected distance from the radula center to the bisecting midline of the jaw, represented as D4 in Figure 4 (reproduced below). This distance is calculated as the difference between the projected distances D2 and D3.

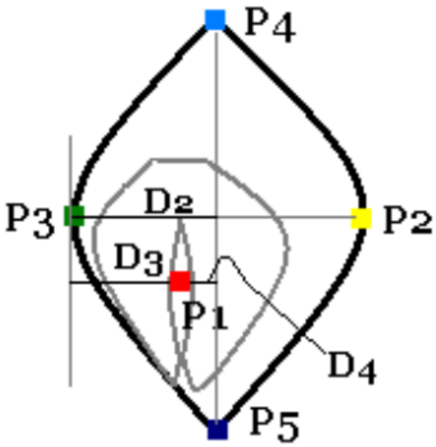

Figure 4. (Reproduced from above) Drawing of jaw and radula with distance and point configurations.

RESULTS

Qualitative results showed that the length of protraction was reduced in the side with a BN2 branch "b" lesion as a result of a reduced force in that side.

Figures 10 – 13 show results from post-lesion behavior of one animal that underwent a unilateral BN2-b lesion. Time zero is approximately when the radula halves close together immediately after peak protraction. The y-axis measures distance in centimeters and the x-axis measures distance in frames (30 frames = 1 second). The length of observation lasted until the points were no longer discernable for plotting in WinAnalyze.

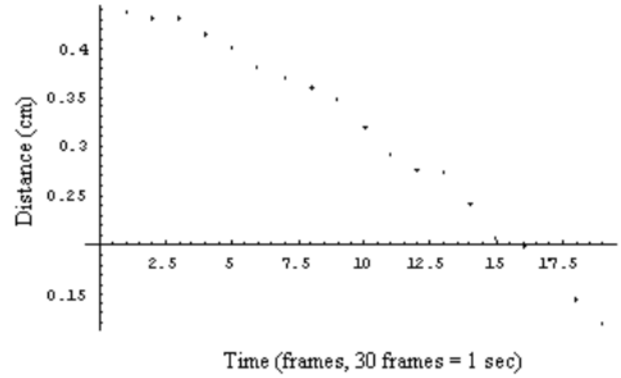

Figure 10. Projected distance (cm) from bisecting midline to jawline along side of mouth as a function of time (frames) for lesioned side. This distance is analogous to D2 defined above.

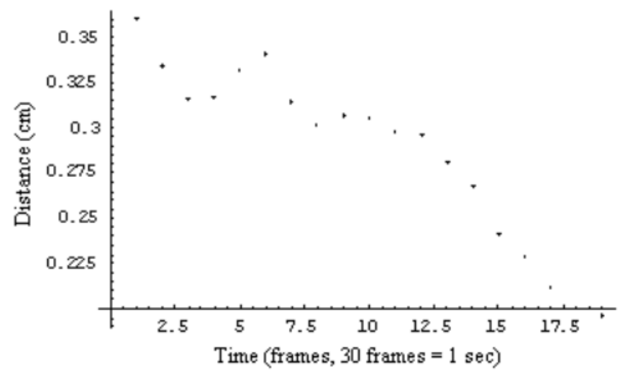

Figure 11. Projected distance (cm) from bisecting midline to jawline along side of mouth as a function of time (frames) for unlesioned side. This distance is analogous to D2 defined above.

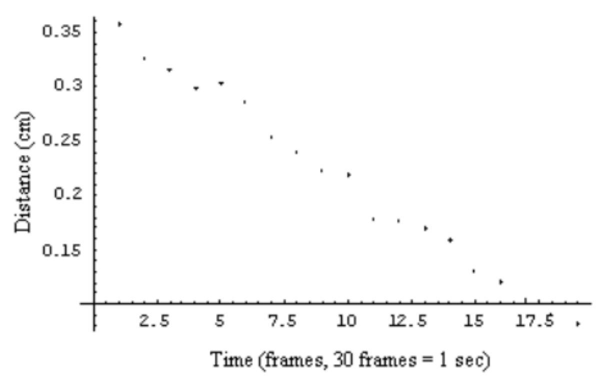

Figure 12. Projected distance (cm) from center of radula to line along side of mouth as a function of time (frames) for lesioned side. This distance is analogous to D3 defined above.

As demonstrated by the graphs above, the lesioned side has a greater rate of change and a greater real change in distance as compared to the unlesioned side. However, comparisons of jaw closure (D2) and radula shift (D3) are difficult to directly compare since changes in these distances may affect each other. Thus, the distances from the radula center to the bisecting midline (D4), or the differences between D2 and D3, were used for analysis and comparison. Figure 14 shows data for the change of D4 over time in the same animal as Figures 10 – 13.

D4 data was compiled for three separate bites from each test animal for both pre- and post-lesion behavior. The distances were then averaged and graphed with standard deviation error bars.

For specimens with a unilateral buccal nerve 2 branch "b" lesion, the pre- and post-surgery behaviors show a significant difference in the amount of radula shift from the bisecting jaw plane midline. As shown in Figure 15, the before surgery average rate of change (slope) was 0.0002 cm/frame, or 0.06 mm/sec. Conversely, the after surgery average rate of change was -1.89 mm/sec (over 30 times greater than the pre-lesion rate of change). For specimens with a unilateral buccal nerve 2 branch "a" lesion, the pre- and post-surgery behaviors did not show any significant difference in the amount of radula shift from the bisecting jaw plane midline. As shown in Figure 16, the before surgery average rate of change was -1.32 mm/sec. Conversely, the after surgery average rate of change was -0.57 mm/sec. The pre-lesion rate of change is not significantly different than the post-lesion rate of change.

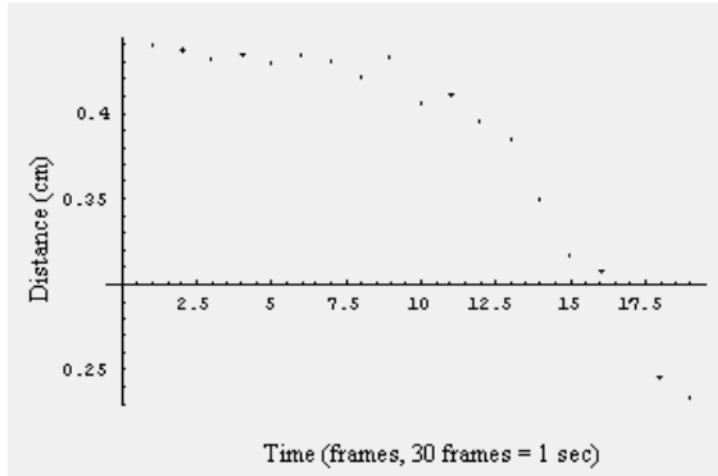

Figure 13. Projected distance (cm) from center of radula to line along side of mouth as a function of time (frames) for unlesioned side. This distance is analogous to D3 defined above.

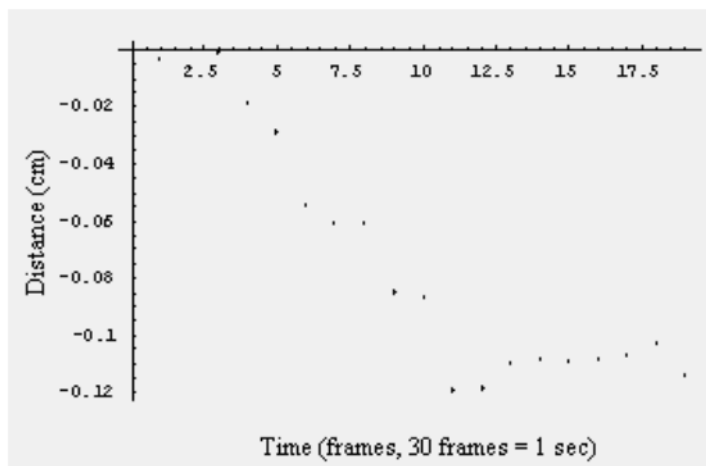

Figure 14. Projected distance (cm) from center of radula to bisecting midline as a function of time (frames) for unilaterally BN2-b lesioned animal. This distance is analogous to D4 defined above.

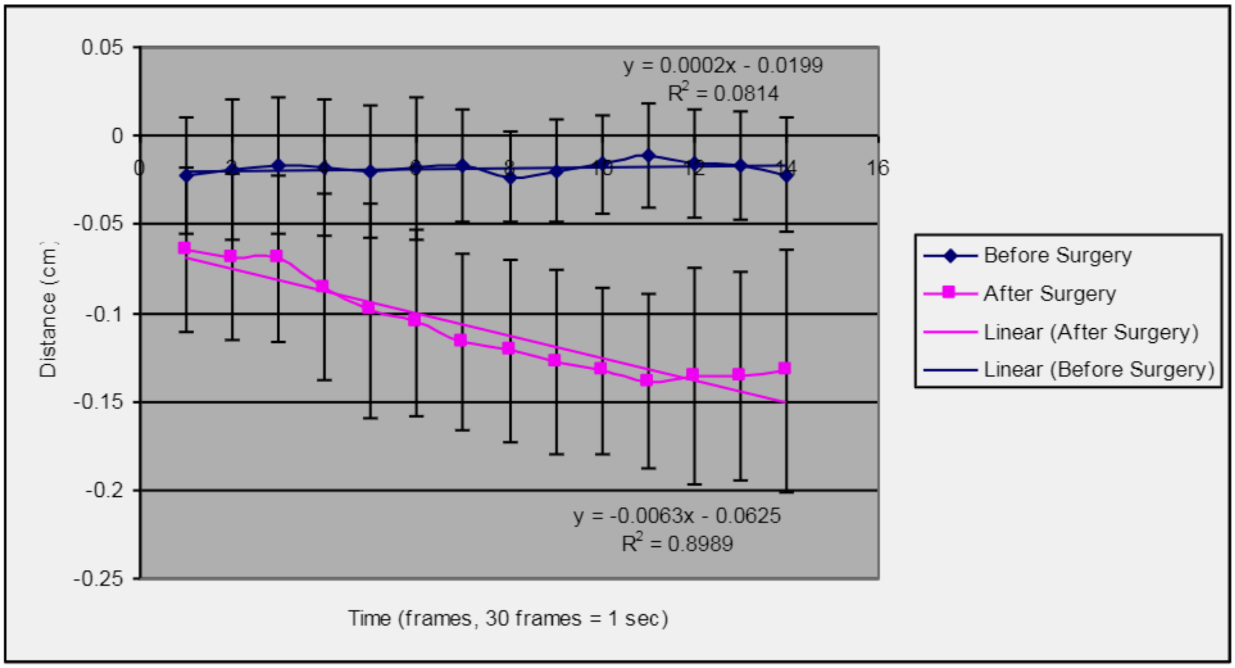

Figure 15. Radula shift distance from the jaw plane midline (D4) during protraction for unilateral buccal nerve 2 branch "b" lesions. This graph is a compilation of data from two sea slugs (N=2), each with three trials for both pre- and post-surgery behavior.

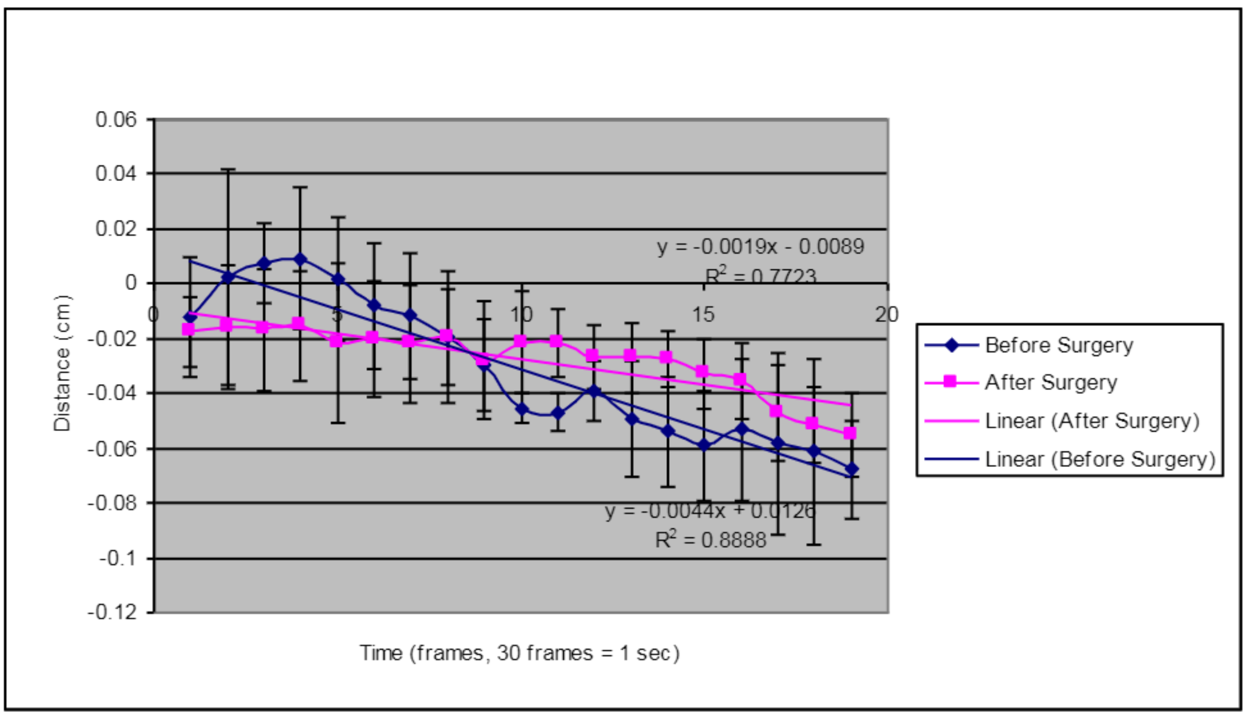

Figure 16. Radula shift distance from the jaw plane midline (D4) during protraction for unilateral buccal nerve 2 branch "a" lesions. This graph is a compilation of data from one sea slug (N=1), with three trials for both pre- and post-surgery behavior.

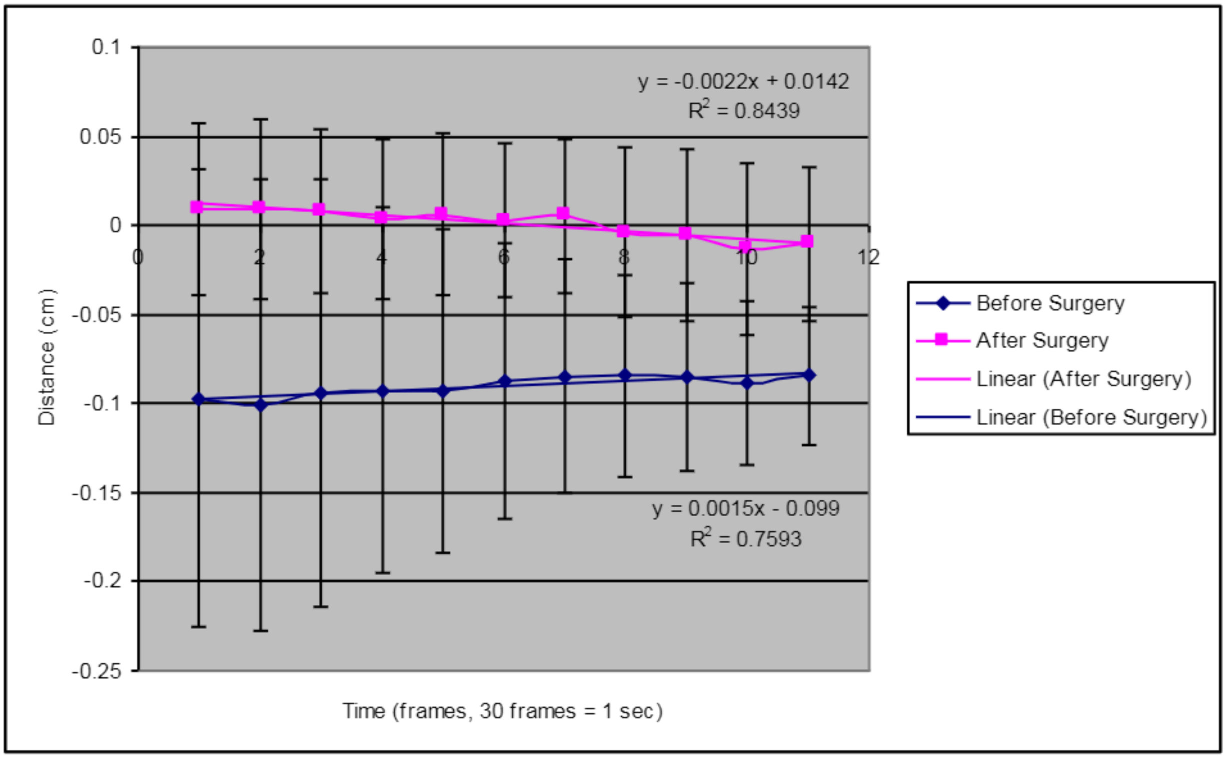

Figure 17. Radula shift distance from the jaw plane midline (D4) during protraction for unilateral buccal nerve 2 branch "c" lesions. This graph is a compilation of data from two sea slugs (N=2), each with three trials for both pre- and post-surgery behavior.

For specimens with a unilateral buccal nerve 2 branch "c" lesion, the pre- and post-surgery behaviors also did not show any significant difference in the amount of radula shift from the bisecting jaw plane midline. As shown in Figure 17, the before surgery average rate of change was 0.45 mm/sec. Conversely, the after surgery average rate of change was -0.66 mm/sec.

Though the initial slope comparison between compiled pre- and post-lesion behavior show significant differences only with a unilateral lesion on BN2-b, there still may be some error in defining significance due to multiple, or unplanned, comparisons. These multiple comparisons include tests of comparisons between all possible pairs of means and introduce error due to possible use of outlying points in the population. To correct for this, we employ statistical comparison of multiple regression lines by first computing the difference between pre- and post-lesion behavior for each test specimen. By calculating the difference in each individual animal as opposed to averaging all data for one particular lesion type, the animal itself is used as its own control. Figure 18 shows an example of this calculation for a single animal.

Furthermore, the observation length is also normalized respective to each individual bite. Normal observation durations vary substantially depending on the number of frames in which the points on the radula and jaw are clearly discernable. Instead of using the least number of frames available for each lesion type, each individual bite observation is normalized by using data

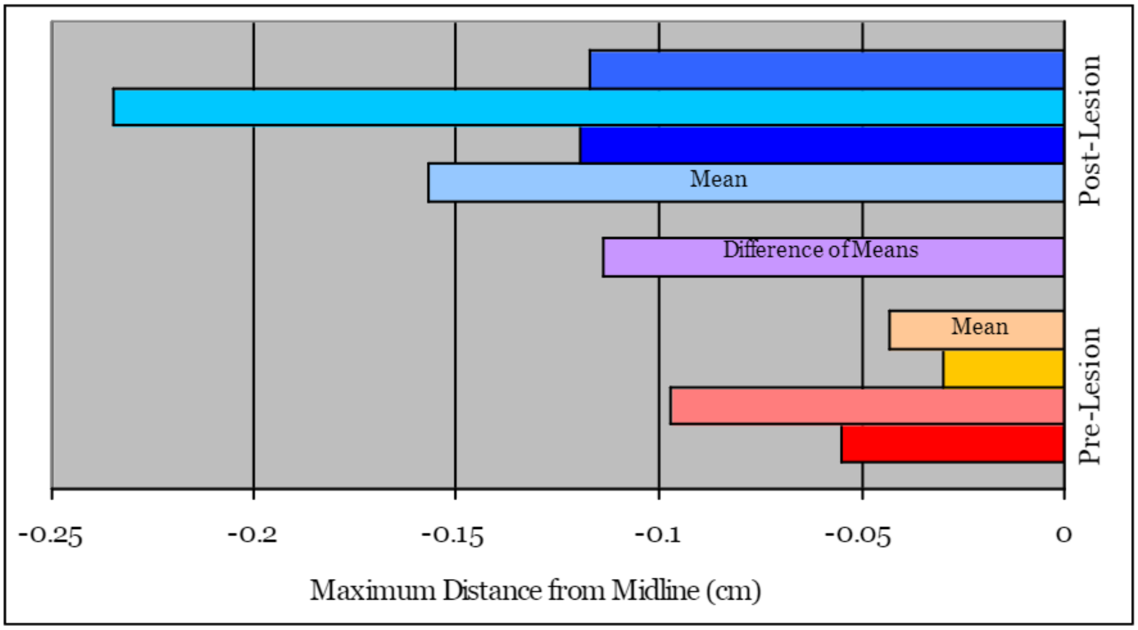

Figure 18. Maximum deviation distance from midline is shown for three bites for both pre-lesion and post-lesion behavior. The difference between the means was calculated as the comparable variable of interest.

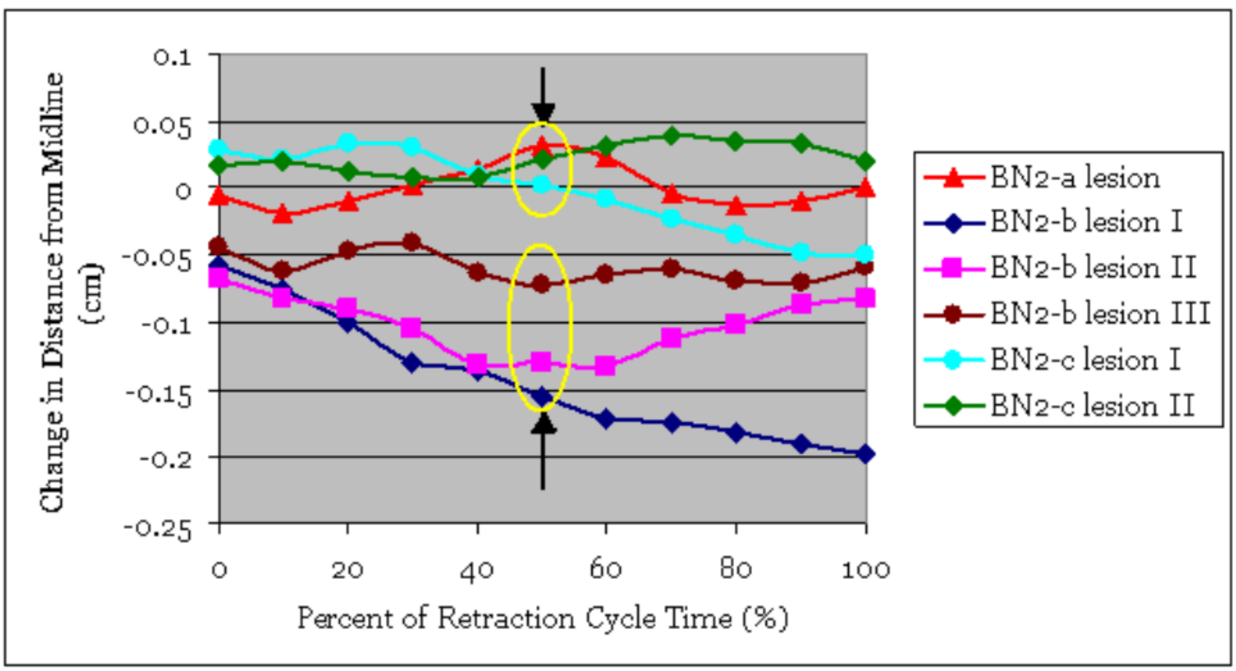

Figure 19. The difference in distance between pre-lesion and post-lesion behavior is plotted along the normalized time scale.

points at 10%, 20%, 30%, etc. of that particular observation. This is accomplished using a point-slope formula. Time at 0% represents when the radula halves close together immediately after peak protraction, and 100% represents when the jaw and/or radula are no longer clearly discernable after retraction.

In addition, observations show that the early phase of retraction (approximately 0% to 50% period) shows a clear deviation of BN2-b shift in comparison to BN2-a and BN2-c lesions. Measurement of the shift from the midline is more difficult due to jaw closure and possible realignment of the midline. In order to test the significance of the deviation at 50% of the retraction cycle time, a one-tailed t-test was performed for two variables of unequal variance. The resulting t-value was 0.01055, and therefore the difference between branch "b" lesions and lesion on the other branches is significant.

DISCUSSION

Unilateral lesions on the branches of buccal nerve 2, responsible for innervation of the I1/I3/jaw complex, were performed to observe the effects on the protractive force during biting. The results support the hypothesis that unilateral lesions on branch "b" specifically would cause deficits in the peak protraction of biting. Furthermore, analysis reveals that unilateral lesions on branches "a" and "c" cause no significant alterations in normal biting behavior.

Normal biting behavior consists of a protraction phase, a peak protraction lasting for an extended period of time, and a retraction phase. Unilateral lesions allowed comparison between behaviors exhibited by each radula half. After BN2-b unilateral lesions, the radula began to retract significantly faster on the lesioned side. Observation of the differences in the distance from the radula center to the jaw plane midline between pre- and post-lesion behavior show that unilateral BN2-b lesions result in an increased retraction (i.e. greater shift of the radula center) towards the lesioned side. The results show that the early phase of retraction in particular clearly demonstrates this shifted behavior. During the late phase of retraction, measurement of the shift is slightly less reliable due to the closing of the jaws and possible re-centering of the jaw plane midline.

Unilateral lesions of BN2 on branches "a" and "c," however, do not show any significant difference in shift between pre- and post-surgery behavior, thus acting as controls surgery. The "b" branch has previously been shown to contract the posterior portion of I1/I3, whereas branches "a" and "c" contract the anterior portion. Thus, these results suggest that forces expressed by the posterior part of the I1/I3/jaw complex are necessary to sustain complete protraction near the peak of biting and slow retraction of the radula/odontophore. Thus, when this active ability is blocked, the impaired side will retract earlier and with a greater rate of change.

In addition to the observations presented in this study, sham lesions were also performed but have yet to be analyzed. Sham lesions follow the same method of anesthesia and surgical procedure as lesioned animals, but a neural lesion is not performed. Analysis of this data will strengthen our confidence in the results observed in control animals, as no neural lesion was imposed. Furthermore, additional statistical analysis, such as confidence intervals, would also aid in determining significant differences in behavior.

Error was one major consideration in the data analysis procedure, especially in the point configuration in WinAnalyze. Though the software has an automatic tracking tool to follow a certain point, there is a large amount of deviation that must be corrected by hand. Future studies may include an additional means to measure deviation from the midline, such as comparing the heights of the radula halves or jaw width. Furthermore, future studies may measure the time from peak protraction to complete retraction in order to quantify the effects of a more rapid beginning of retraction (due to the lost protractive force).

These studies are helpful in further understanding the interactions between biomechanics and neural control not only in invertebrates such as *Aplysia*, but also other organisms in which muscle performs both force and skeletal support functions, i.e., tongues, trunks or tentacles. In particular, study of the neural control over context dependent muscles in *Aplysia californica* can provide insight into those of other organisms. As shown by previous studies, human muscle may also exhibit context dependent behavior. For example, elbow flexion deviation and postural variation can occur as a function of its context. The results of studies on invertebrates can be used towards understanding muscular function in humans and higher order animals. Furthermore, this understanding could be applied to the research and development of mechanical devices to replace muscles. For example, current research on prosthetics has focused on functional electrical stimulation (FES) to restore movement, sight, and other normal capabilities (Faghri *et al.* 1994 and Marsolais *et al.* 1987).

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