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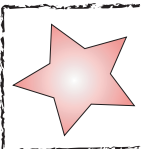
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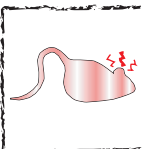
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Letter from the Editor

Dear Readers,

Welcome to the inaugural issue of the University of Michigan Undergraduate Research Forum. As a cross-disciplinary undergraduate research journal, we aim to showcase the wide range of student research activities situated on our campuses. As this issue premieres, more than ten thousand undergraduates are engaged in research through the Undergraduate Research Opportunities Program (UROP), individual departments, or independently. It is the goal of the Forum to join various local symposia, poster sessions, and lecture series in making this research more accessible to all.

We intend the Forum neither to act only as an outlet for experienced student researchers, nor a gateway for newcomers, but rather as an anchor to pull both types of undergraduates together. It is our hope that while laboratory veterans fine-tune their written presentations for publication, freshmen will flip through these pages to catch a glimpse of future opportunities. For every student who seeks to explore an unfamiliar discipline, a peer seeks an opportunity to teach it and to form fresh perspectives on familiar topics.

We encourage active student involvement in the Forum: students of any field of research are invited to submit letters, articles, and reviews for publication. We also welcome diverse talent to our staff.

We hope readers can find something in these pages to spur fresh insights and participation in the broader academic dialogue.

Sincerely,



Wei Gu
Editor-in-Chief

Dear University of Michigan students and faculty,

The University of Michigan takes great pride in providing significant opportunities for undergraduates who wish to engage in serious research. The Undergraduate Research Opportunity Program and the Women in Science and Engineering program are two examples of nationally recognized efforts to integrate research and undergraduate education. With this first volume of the Michigan Undergraduate Research Forum, our University takes a natural step forward in extending undergraduate involvement in research to the publication of a journal — with articles written by students, article selection and review guided by students, and journal operations overseen by students. I was very pleased when I first received the proposal for the Michigan Undergraduate Research Forum, and am today doubly pleased to see the process completed with the first issue now published. I hope this will be the start of something very special on our campus.

Best regards,
Fawwaz T. Ulaby
Vice President for Research



Interview with Fawwaz Ulaby, Vice President for Research

Dr. Fawwaz Ulaby is the Vice President for Research at the University. Over the course of his career, he has worked and taught at both the universities of Kansas and Texas at Austin. In 1984, he came to Michigan as a professor of electrical engineering and computer science. In 1999, Ulaby was appointed the VP for research at OVPR. During his tenure, research expenditures have gradually increased. Over the past year, expenditures increased 14.3%, the largest proportional increase since 1987.

Ulaby's immense respect for the University's faculty and students is quite evident. "The reason we have been so successful is because of the creativity of our faculty, the outstanding support provided by our staff, and the imagination and perseverance of our students," Ulaby once said.

In an exclusive interview with the vice president, the Undergraduate Research Forum questioned Ulaby on research, the administration and the value of student participation.

What do you feel is the University's greatest asset in its research? Federal funding, faculty, or its size?

The single most important aspect of the University that explains its success is its people, specifically, the faculty, staff, and students. It is the quality of the people, their zest for asking difficult questions and probing complex problems, being able to look at them through the lenses of the different disciplines and trying to understand the interrelationships between the various disciplines, that makes this research at the University succeed. That then brings the federal funding, brings the interest on part of the students to pursue discoveries, brings in the facilities and everything else that comes with it. The role of the administration is to facilitate and make it happen.

How do students fit into the University's research framework?

At the graduate level, research is integral to a student's experience. Usually, you do a thesis or some sort of a research project, and therefore research and graduate education are linked. You can't separate one from the other.

At the undergraduate level, it takes various forms. UROP is a perfect example where some 1,000 students take advantage of the program, explore research opportunities and ways of learning about what research really is. Also, many schools, colleges and department across the campus have their own research programs. So my guess is that another 1,000-2,000 students take advantage of those resources to explore what research means. What's neat about this whole process is that so many faculty members across the campus are willing and interested to sit down and work with undergraduates going through this discovery process.

In which field(s) do you feel we are strongest?

There are two types of universities across the country. There are universities where things are average across the board, and then they have a few pinnacles where their work stands out. There are universities like Michigan and Berkeley, which are strong essentially across the board. Every single school and college on campus basically rates in the top ten or fifteen in the country. That says that the students, no matter what discipline they chose, are working with some of the best faculty in the country.

What field(s) are we looking to expand or improve, with a particular focus on "expand"?

"Expansion" may not be the right term. The nature of knowledge and discovery is "extension" and

not so much “expansion”. The more you learn the more you want to extend your knowledge into deeper or new directions, because you have already unearthed what you have discovered. Every discipline across is campus is trying to do this. They are trying to establish where the new questions are, where the new challenges are, and how to go after them. As for the size of the University, we’re really not growing in terms of the student or faculty size, but we are expanding our knowledge horizons.

Finally, what are your feelings on the Undergraduate Research Forum? What merits do you see in it?

If I did not believe in it 100%, I would not have used funds from this office to support it, to make it

become a reality. I think it’s a wonderful idea for undergraduate students to describe the results of their research, to write it up, and to start the process of communicating their findings—that is usually the realm of graduate students. There are numbers of schools across that have programs like this. Some of them are very successful. So, I’m very glad to see that there are group of students at the University who are interested in launching this program and making it succeed. I wish them all the success in the world.

Contributed by Aymar Jean

News Briefs

Scientists discover how anthrax creates spores

Researchers at the University of Michigan, The Institute for Genomic Research (TIGR), and Scripps Research Institute have discovered the genes and proteins responsible for spore formation by the *B. anthracis* bacterium. Anthrax spores are capable of withstanding harsh conditions for decades before germinating and allowing the deadly bacteria to infect a new host. The researchers found that as many as one third of all *B. anthracis* genes are devoted to spore formation, and that these genes are expressed in five phases over a five-hour period. The spores produced are much more complex than those of other bacteria, being made up of about 750 proteins apiece. The study, the first investigation of a bacterial pathogen to combine proteomics and genomics, was the cover story of the Jan. 1, 2004 issue of the *Journal of Bacteriology*.

Burning fossil fuels shown to increase reflectivity of clouds

The first direct observational evidence that burning fossil fuels contributes to climate change by increasing the reflectivity of clouds was published in the Jan. 15, 2004 issue of *Nature* by researchers at the University of Michigan and the University of North Dakota. The researchers compared atmospheric data from Oklahoma, which has high levels of aerosols produced by burning fossil fuels, and Barrow, Alaska, which has low aerosol levels, to show that the difference in cloud reflectivity between the two sites was due to aerosol concentration. They also showed that the computer model used to predict cloud reflectivity based on aerosol levels was valid, and that increased cloud reflectivity in areas with high aerosol levels caused cooling of the climate. However, they cautioned that this cooling would be small compared to the heating caused by the increased levels of carbon dioxide in the atmosphere.

Researchers able to predict distribution of endangered species

A research team including two members of the University of Michigan Museum of Zoology has developed a computer model to predict the distribution of endangered species. The model combines satellite remote sensing data and information from specimens in museum collections to predict the current locations of the species. Knowing the distributions of endangered species is important to conservation efforts, but such information was previously difficult and time-consuming to obtain. The new model had a success rate of 75 to 85 percent in predicting where 11 species of chameleon would be found in Madagascar, and also predicted chameleon populations in areas where seven previously unknown species were later found. The test of the model involving chameleons was published in the Dec. 18, 2003 issue of *Nature*.

Studies suggests brown dwarf stars may form in same way as sun-like stars

Recent studies by a University of Michigan astronomer and collaborators provides evidence that brown-dwarf stars retain dusky discs long after the stars first form, suggesting that they may form in the same way as more massive, sun-like stars. In the past, there has been some debate whether brown dwarfs form, like normal stars, by accumulating matter from clouds of dust and gas, but simply don't accumulate enough to ignite nuclear fusion; or whether they are ejected from systems where multiple stars are being formed. In the second scenario, the other stars could be expected to strip away the dusty discs surrounding the brown dwarfs. The researchers were able to find the dusty discs around the majority of young brown dwarfs, suggesting that they form in the same way as normal stars.

Decline in teen smoking slows

Findings released by the University of Michigan Institute for Social Research (ISR) in December show that the decline in teen smoking has begun to slow. Cigarette use among teens has been dropping since the mid-1990s, but the declines among 8th- and 10th-graders in 2003 were not statistically significant. The decline among 12th-graders was significant, but researchers believe it can be attributed to the decline in smoking at lower grade levels when the current 12th-graders were younger. Smokeless tobacco use is also declining among teens, but that decline too has slowed. Results also showed that increasing numbers of teens reported that they prefer to date people who do not smoke. The percentage of teens who reported that cigarettes were “easy to obtain” is steadily decreasing; however, the majority do think that cigarettes are easy to obtain. In 2003, 10 percent of 8th-graders, 17 percent of 10th-graders, and 24 percent of 12th-graders reported smoking in the past 30 days. Nearly 500,000 students from across the nation were surveyed as part of the “Monitoring the Future” studies by the ISR.

Astronomers find clues to origins of high-velocity neutral gas clouds in Milky Way

Two University of Michigan researchers studied high-speed clouds of neutral hydrogen gas in two nearby galaxies, which allowed them to find the approximate mass and distance of the clouds. The Milky Way contains similar clouds which move at much higher speeds than the stars and normal clouds of gas. The high-speed clouds of neutral gas make up about 1% of the gas contained in a galaxy. However, the masses and distances of these clouds in the Milky Way are not known. The researchers used radio waves to investigate the clouds in nearby galaxies, and assumed that the distances to the clouds were approximately the same as the distances to the galaxies. Assuming that the Milky Way has the same amount of high-velocity gas as the nearby galaxies, the high-velocity gas clouds lie on the halo of our galaxy. This suggests that the gas clouds may have been formed when other galaxies passed nearby, their gravity pulling the gas away from the Milky Way in long ribbons. The findings were presented at the 203rd meeting of the American Astronomical Society in Atlanta, Georgia on Jan. 8.

Study finds substance use still common at age 35; high school substance use predicts use as adults

Studies conducted annually since 1975 at the University of Michigan Institute for Social Research (ISR) show that heavy drinking and drug use is more prevalent among 35-year-olds than might be expected, and that participants’ high school substance use patterns may predict their substance use later in life. The findings, published in the Jan. 2004 issue of the American Journal of Public Health, show that more than 32 percent of men report drinking heavily—five or more drinks in a row—at least once within the last two weeks, while almost 13 percent of men and 7 percent of women have used marijuana in the last month. 7 percent of men and 8 percent of women reported misusing prescription drugs in the last year. The researchers also found that men and women who had used cigarettes, marijuana or illicit drugs, or who drank heavily, during high school were more likely to use the same substances at age 35. It was also found that men and women who were married were much less likely to report drinking heavily or using illicit substances, while those who had graduated from college were less likely to report drinking heavily. Custodial parents were less likely to report substance abuse, though 29 percent of custodial fathers reported drinking heavily, and custodial parents were just as likely to smoke or misuse prescription drugs as non-parents.

Information obtained from www.umich.edu/news/releases.html

Literature Searching Online using the University Library

Only two decades ago, a researcher needed to perform any literature searches through bookshelf archives of scholarly journals. The modern researcher can now look for most recent journal manuscripts online from the comforts of the laboratory or research setting. Expansion of the Internet has made finding and obtaining research articles faster and easier.

Literature searching is an important part of most research activities. It is a waste of time and effort to reinvent what is already patented, or rediscover what has already been uncovered. To find articles of interest, many researchers use online databases to locate citations and abstracts. Popular databases include ProQuest for humanities and social sciences, ISI (Institute for Scientific Information) Web of Knowledge for natural science and engineering, and PubMed for medical science. These databases not only locate interesting articles through searches based on keywords, titles, and author names, they also have extra features. Some include search algorithms

for related articles (PubMed), or lists of other related works that have cited a certain article of interest (ISI).

Obtaining the actual papers from a list of relevant citations can also be challenging. There are thousands of journals available, not to mention reference books, conference proceedings, and patents. Some are free to access, but more carry a fee. Fortunately, as one of the top ten North American academic libraries, the University Library has access to almost all of the popular search databases and journal carriers (Association of Research Libraries Statistics, 1992-2002). Databases are usually located under "Networked Electronic Resources," and links to online journal carriers can be found under "Electronic Journals and Newspapers" on the Library webpage.

While some journal carriers such as Wiley Interscience and American Chemical Society Publications centralize their article collection, journal carriers typically are not compatible with each other,

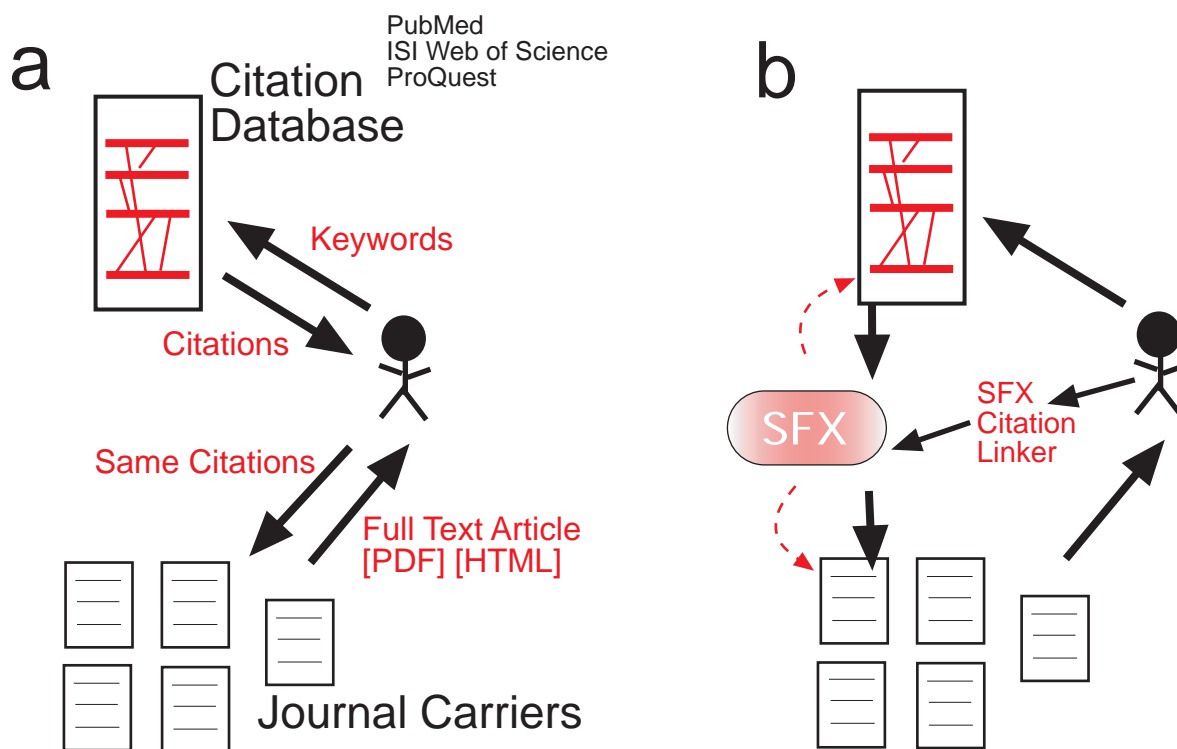


Figure 1: In (a), a literature-searching student enters key terms in the citation database and gets a list of citations. Using these citations, full texts can be obtained individually. In (b), the University Library's SFX automates communication between citation databases and full text carriers.

and it can be time-consuming to surf online through several different journal carriers for papers on the same topic. Recently, the University Library installed a new online service called SFX, an abbreviation for “special effects”. This service further automates literature searching by acting as a negotiator between the research user, online databases, and online journal carriers. SFX can automatically read the citation of the article of interest and link the user as close as possible to the full article location. Although medical researchers already have a similar service through PubMed, SFX is more universal and can automate a link from other large databases such as ISI Web of Science to specific articles. While SFX is limited by differentiated access to different online citation databases or full text articles, it can still be a time saver if researchers are ready to use previous literature searching methods as a failsafe.

For further information, students and researchers can speak directly to a librarian, chat online with a librarian through the “Ask Us” program, try the Research Consultation Program, or see the Science Research Advisors.

For more information, see:

SFX - <http://www.lib.umich.edu/help/sfx/>
Ask Us - <http://www.lib.umich.edu/askus/>
Research Consultation Program - <http://www.lib.umich.edu/ugl/services/rcp/index.html>
Science Research Advisors - <http://www.lib.umich.edu/science/reference/scirescon.html>

Contributed by Wei Gu

American Customer Satisfaction Index (ACSI)

Established in 1994, the American Customer Satisfaction Index (ACSI) is a uniform and independent measure of household consumption experience. A powerful economic indicator, the ACSI tracks trends in customer satisfaction and provides valuable benchmarking insights into the consumer economy for companies, industry trade associations, and government agencies. In 1995 Thomas A. Stewart wrote that customer satisfaction is so central it can be actually said to define economic activity: “An economy cannot be described by adding how many tons of rebar it makes, how many passenger miles of air it logs, or how much a woodchuck chucks per hour. All these count (and we count them), but in the final analysis what matters is how well an economy satisfies its customers.” [1]

The ACSI is produced through a partnership of the *University of Michigan Business School*, the American Society for Quality (ASQ), and the international consulting firm, CFI Group. The University of Michigan established the National Quality Research Center (NQRC) in its business school to complement traditional economic indicators with a measure of the quality of economic input. Professor Claes Fornell, who teaches business administration, is the director of the NQRC at the

University of Michigan Business School and chairman of the CFI group, Ann Arbor, MI.

ACSI Methodology and Processes

The ACSI reports scores on a scale of 0 to 100 at the national level. The areas covered by ACSI include 7 economic sectors, 39 industries, 200 companies and federal or local agencies. It also produces scores for the cause and consequences of customer satisfaction and their relationships.

Data is collected via telephone interviews with the customers. For e-commerce and e-business, customer interviews are conducted via the Internet. From random-digital-dial telephone samples, more than 65,000 consumers are identified and interviewed annually.

Since 1994, data from more than 500,000 customers has been amassed.

Customer Expectations:

Expectations are measured by combining customers’ experience with a product or service and information about it via media, advertising, salespersons and word-of-mouth from other customers. These influence how successful the product or service will be?

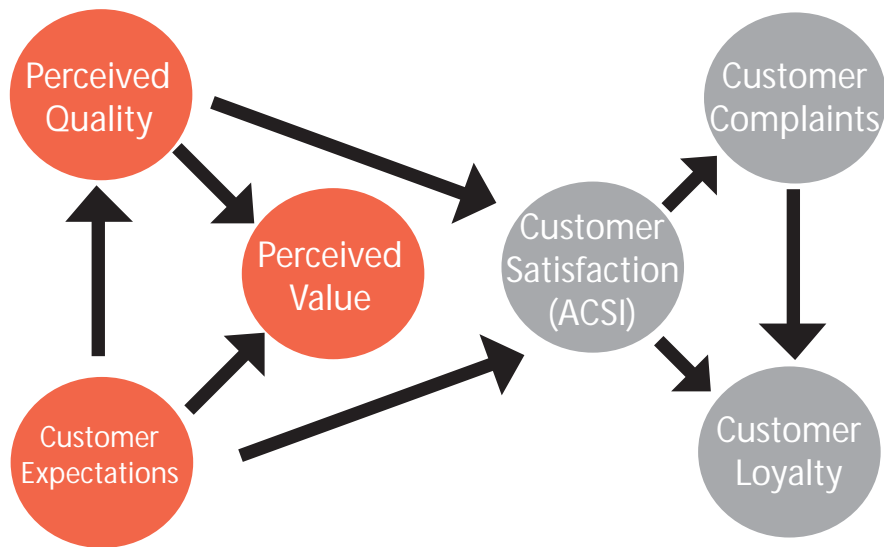


Figure 1: The model [2] for the private sector. The government agencies' model works along nearly the same lines.

Perceived Quality:

This is measured through three questions: overall quality, reliability and the extent to which a product or service meets the customer's needs. Perceived quality proves to have the greatest impact on customer satisfaction

Customer Complaints:

Customer complaint is measured as the percentage of respondents who reported a problem with the measured companies' product or service within a specific time frame. Satisfaction has an inverse relationship to complaints.

Customer Loyalty:

Customer loyalty to a particular brand is measured through questions on the likelihood to purchase a product or service at various price points. Satisfaction has a positive effect on loyalty.

Predictive Capabilities

ACSI's predictive ability comes from its use of a cause-and-effect econometric model that links customers' evaluations of their experiences with products and services to their overall satisfaction. The ACSI satisfaction index is linked in turn to key behavioral consequences of satisfaction – customer retention and price tolerance. See figure 2. [2]

A basic tenet of the ACSI is that satisfied customers represent a real, albeit intangible, economic

asset to a firm. The modern economy – characterized by service and information exchange – calls for measurements of intangible assets critical for economic returns. The ACSI is a tool that allows customer managers and investors to relate satisfaction to future streams of income.

Joseph White, the dean of the Michigan Business School in 1994, explains ACSI as a vital new tool for economic performance. "For the first time" he said "we will have a reliable measure of quality of goods and services consumed in our economy. And for the first time, we will enable the voice of the customer to be heard in economic measurement." [3]

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2. www.theacsi.org
3. Claes Fornell. "Boost Stock Performance, Nation's Economy" *www.asq.org*, Feb. 2003.

Contributed by Shahzad Zafar



Figure 2: ACSI: A Predictor of Corporate Earnings. Research by faculty at the University of Michigan Business School shows that corporate earnings and ACSI scores are correlated. The ACSI from one period of time is predictive of the change in earning for the following period. The reason is that a satisfied customer is more profitable than dissatisfied one. If satisfaction declines, customers become more reluctant to buy unless prices are cut. If satisfaction improves, the opposite is true: customers are more inclined to buy again and are less sensitive to price increases.

Life Sciences Institute Provides Students and Faculty with New Facilities

With the opening of the Life Sciences Institute this fall, students now have a new outlet for conducting biological research at the university. The new LSI building is located on Washtenaw across from Palmer field, and connects the university's central campus with the medical campus via a pedestrian bridge.

Currently nine scientific investigators have been recruited as faculty in the Life Sciences Institute. A total of nine faculty now have their laboratories in the LSI building and a total of twenty to thirty faculty are expected. Dr. Alan Saltiel, director of the Life Sciences Institute, says the LSI's goal has been to

“recruit outstanding faculty, who are interested in a highly collaborative environment.” These faculty have been chosen by leaders of the university interested in cultivating the success of LSI from a seed of experienced investigators. Dr. Kunliang Guan was among the first faculty to move into the LSI; he pointed out that the move into the LSI building was a “quick transition” and that everyone in his lab likes the new space. Dr. Guan moved from the Medical Sciences Building I.

According to Dr. Saltiel, the university plans to attract scientists from outside the university to the

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facilities provided by the LSI building. Dr. Guan agreed and stated that as a faculty member of the LSI, his most emphasized additional responsibility is in the recruitment of other faculty. While the institute's goal is not to maintain "cutthroat" competition with other universities, the institute is intended to serve a competitive purpose in a fast-paced field both in recruiting faculty and making scientific contributions. Dr. Guan remarked that he plans to work closely with Drs. Ginsburg and Margolis while maintaining strong interaction with faculty outside of the institute as well. National and international cooperation are also being encouraged, one such example being the institute relationship with the Weisman Institute in Israel.

According to Dr. Saltiel, the focus on the life sciences is the result of a sharp change in tools coupled with a multitude of unanswered questions. Specifically, he described the sequencing of the human genome as a "quantum leap" which the university was not able to keep up with, previous to the inception of the institute. Dr. Guan said that the university will "definitely" advance with regards to biological research thanks to the institute, though a timeframe of ten years before such an advance might be appreciated would not be surprising.

Faculty conducting research in the Life Sciences Institute maintain their previous departmental affiliations—they teach courses through their respective academic departments. This is due in part to the fact that the institute does not serve an academic purpose in the classroom setting, said Dr. Saltiel. Rather, it is intended to serve as a research oriented program within the university. The lack of a class-oriented academic program and the highly collaborative nature of the institute distinguish it from other academic

departments such as chemistry or biology. Dr. Guan stated that the LSI building is divided on the basis of biological field on a floor-by-floor basis. The third floor is reserved for structural studies, the fourth for a chemistry-oriented approach, and the fifth and sixth floors for an interest in molecular genetics.

Dr. Saltiel conducts research in cellular biology, specifically signal transduction. One of the goals of his research is to learn how hormones control metabolism, an example being the hormone insulin; his lab has also discovered several genes. Dr. Guan's laboratory is interested in studying a biochemical approach to learning about cell growth and cell size regulation.

Students who are interested in getting involved with research at the institute should go online to www.lifesciences.umich.edu/institute. There they can learn about different faculty and their respective research interests. Dr. Saltiel suggests that the best method of contact is via e-mail. Students interested in working at the building this summer should find out about the Perrigo Fellowship, an elite program which will be open to students across the state starting this summer.

Contributed by Shailesh Agarwal

Fluorous Chemistry

Developing more efficient catalysis of reactions, separating products from byproducts, and devising more environmentally friendly reactions are some of the issues that chemists face every day. Fluorous chemistry is an emerging branch of chemistry that provides alternative solutions to many of these problems. "Fluorous" is a term analogous to "aqueous" [1], describing a new class of molecules in which fluorine atoms take the place of hydrogen atoms, generating new and interesting properties. These properties make fluorous chemistry suitable for far-reaching applications in separations and catalysis, as well as for industrial application in LCD displays.

Fluorous chemistry begets a "parallel universe" of organic molecules [2], with new and versatile properties that can be exploited in a number of ways. These molecules include fluorous solvents and fluorous-tagged molecules, which generally contain an organic region, containing the reaction center, and a fluorous region, which dictates solubility (see Figure 1). Scientists can adjust properties by altering the fluorine content, as well as altering the number of so-called methylene spacers between the fluorous domain and the organic domain. Such versatility allows scientists to fine-tune properties for specific applications.

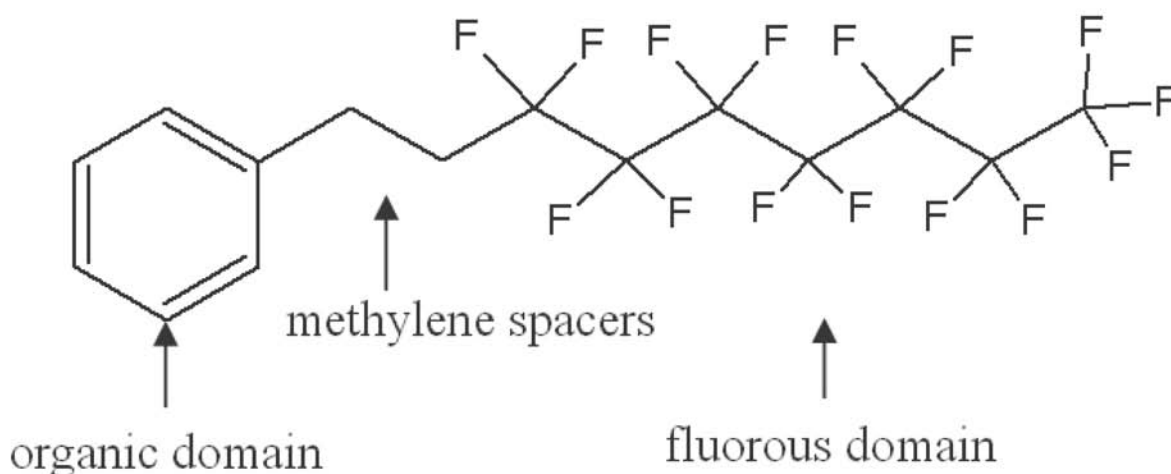


Figure 1: An example fluorous molecule

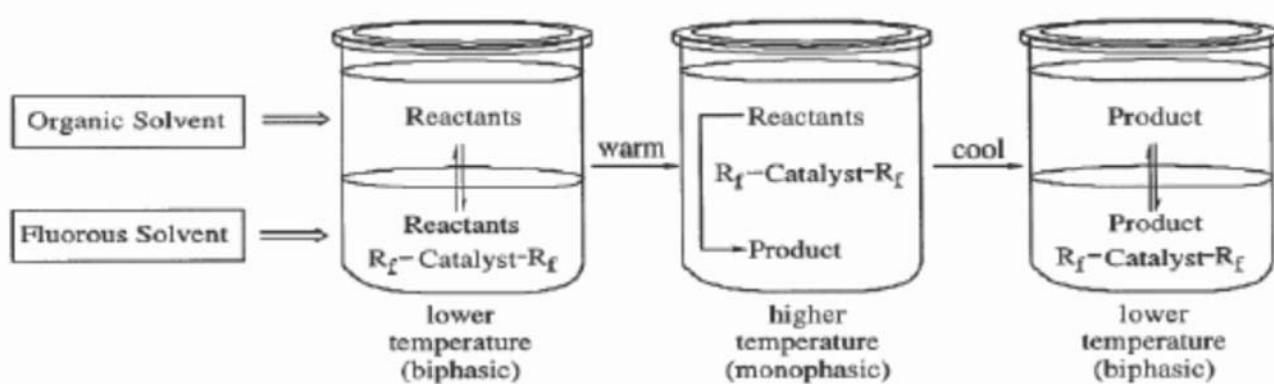


Figure 2: Fluorous biphasic catalysis [3]

One primary application of fluorous compounds is in separations and catalysis. This stems from the fact that many fluorous compounds and solvents are not miscible with organic or aqueous layers at room temperature. A common problem in heterogeneously catalyzed reactions is the inefficiency of the catalyst, which is in a separate phase from the reactants. Fluorous biphasic catalysis poses a novel solution to this issue by bringing the catalyst into the reaction phase and then allowing its easy removal. As shown in Figure 2, a fluorous catalyst dissolved in a fluorous solvent is placed into the reaction chamber, along with reactants in an organic phase. The reaction vessel is heated, causing a monophasic to form, and allowing the reaction to take place at high yield. Then the mixture is cooled, and the fluorous/organic biphasic re-forms, allowing for simple liquid/liquid extraction

to isolate the product and recover the catalyst for reuse.

The method just described demonstrates the potential for liquid/liquid and liquid/solid extraction procedures that fluorous chemistry creates. Liquid/liquid extraction can be utilized to purify a product in an organic phase when reactants, byproducts, or catalysts are fluorous. Solid/liquid extractions are being used in the form of fluorous silica columns, and also can be used to avoid column chromatography to separate a solid fluorous product [4].

A related idea for research, which follows the theme of "green" or environmentally friendly chemistry, is the engineering of reactions with minimal byproducts and waste. As discussed earlier, fluorous chemistry allows for higher yield reactions and easier separation. There is on-going research in the development of new fluorinated catalysts, particularly

solid, fluorous catalysts, which go into the liquid phase at higher temperatures and then fall out of solution when cooled, as reported by Gladysz [5]. These catalysts would allow for high yield, homogeneous catalysis. It is less harmful to the environment and more economical when less waste is produced and the product and catalyst are recovered more easily.

Further, despite the reputation of halogenated compounds as toxic, ozone-depleting agents, many fluorinated solvents are proving to be non-toxic [6]. Besides fluorous solvents, researchers have developed fluorous reagents, which have proven more environmentally sound. Scientists at the University of Chicago have run a fluorous Swern reaction giving fluorous dimethyl sulfide as the byproduct as opposed to the environmentally hazardous dimethyl sulfide [7]. The fluorous form is high-boiling, odorless, and can be easily recycled [7].

A second idea for research is the synthesis of fluorous compounds in search of liquid crystals, or non-linear optical properties stemming from the unique intermolecular forces characteristic to fluorous molecules. Liquid crystals are neither solids nor liquids; they flow like liquids, but the molecules form ordered arrangements like solids. For years, scientists have developed transition metal-containing compounds that have exhibited liquid crystalline properties [8]. Recently, they have synthesized fluorous analogs to such compounds, and have observed even better liquid crystalline properties [9]. There is much promise in the synthesis of fluorous analogs to many compounds and metal complexes with a wide variety of metal cores in search of non-linear optical properties. Further, there is potential for the implementation of such compounds into the liquid crystal display industry.

Fluorous chemistry is a burgeoning field of chemistry with potential to improve separations and catalysis, to make reactions more environmentally friendly, and to revolutionize the liquid crystal industry. Scientists and engineers constantly seek methods to improve the efficiency of processes and at the same

time reduce environmental pollution. The unique properties of fluorous molecules have led to new solutions to such problems. As the potential of fluorous chemistry is fully realized, it is likely to become ever more pervasive in research and industry.

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Contributed by Dan Schmidt

Microfluidics: Tiny Streams with Huge Potential

Microfluidics, the study and utilization of small volume fluidics, is a rising cross-disciplinary field. At the University of Michigan, research groups from a number of different departments use this technology. These departments include chemical, biomedical, and mechanical engineering; applied physics; analytical chemistry; human genetics; assisted reproductive technologies; and tissue engineering. What makes microfluidics useful to these fields? The answer lies in the goal of shrinking large biochemical facilities into “lab-on-a-chip” devices. Optimistic parallels are often drawn between microfluidics and the rise of the personal computer. Decades ago, a single computer took up more than a room; today, we have Pocket PCs. Having such a lab-on-a-chip device would then be like owning a Pocket Lab [1].

As microfluidics gained popularity, interesting phenomena were observed, encouraging the exploration of new possibilities not possible on a larger scale. One that was of particular use is the “invisible wall” phenomenon, which allows two streams within a tiny channel to flow parallel to each other without mixing. The phenomenon can be explained by fluid mechanics laws that ensure liquid flow in small radius channels is laminar, and will not mix due to absence of turbulent eddies. This phenomenon has been taken advantage of by researchers such as Shuichi Takayama’s group (biomedical engineering). The group has exposed single cells to two different parallel streams of reagents to study single cell responses, and also to allow viable sperm cells to swim away from idling dead sperm cells into a parallel flow fluid, separating purified viable sperm for in vitro fertilization [2].

Jens-Christian Meiners’ group (physics) has also taken advantage of non-turbulent, small-scale fluid flow by studying single strands of DNA anchored in microfluidic channels. They then use optical tweezers to gingerly move individual strands without large random disturbances from the surrounding liquid.

Another inherent advantage of working small is low sample or reagents consumption. When all three length dimensions are decreased by a factor of 10, the corresponding volume change is a decrease not by a factor of 10, but rather 1000. For example, if we decrease the width, height, and length of a macroscopic channel by a factor of 100 each way, the amount of fluid needed to fill the original macroscopic channel will fill one million of the smaller channels. In other words, it is now possible to use

just one millionth of the material that was previously needed. For expensive and rare biochemical preparations, this turns out to be a powerful advantage.

The field of microfluidics is constantly evolving, and several approaches have been found to be viable for fabricating tiny, hollow channels and driving fluid flow through them. Early microfluidics researchers borrowed photolithographic technology from the semiconductor industry to etch miniaturized channels (.001-1 millimeters) on silicon or glass wafers. (Photolithography is also used to pattern DNA on popular Affymetrix Chips [3].) These capillary channels are essential to delivering nanoliters and sub-nanoliters of liquid (a nanoliter is a billionth of a liter, and a millionth of a milliliter). A later technique, called Soft Lithography, involves polymerizing liquid monomers on photolithography-patterned substrates to create rubbery replicas with channel features.

Research in the microfluidics field has centered on the fabrication and demonstration of individual components, the integration of these components into working devices, and application of these devices to biology and chemistry. In the past, most of the work was done on the individual components, and applications often did not provide an equal balance. Recent work has increasingly focused on the integration and application of the components. For example, Mark Burn’s group has a device that sends DNA through PCR and electrophoresis [4]. This device not only commands nanoliters of fluid flow, but also contains a chemical reactor and separations unit. One can imagine the possibilities of such a device as a mobile bioanalytical device.

For additional information, visit the Microfluidics Interdisciplinary Workshop at the University of Michigan:
<http://sitemaker.umich.edu/microfluidics>

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Contributed by Wei Gu

Zero Tolerance Policies: Ineffective Discipline Pushing Students Out of School

Kelly Alexander

Students in Southwest Detroit have sighted problems with the harsh discipline policies in their schools that are a product of zero tolerance. Zero tolerance is a policy that was developed in order to protect students while in school, however the policy is pushing students out of schools and depriving them of their education. The purpose of this research is to further understand the effects of zero tolerance on Southwest Detroit high school students. The findings suggest that students are concerned discipline is unclear and that their schools are not supporting them or preparing them for their futures. Proposed recommendations include the formation of peer juries and the involvement of students in the decision-making process.

Two West Bloomfield High School girls fight on school grounds and as a result are sent to the principal's office. The students are allowed to explain what occurred and are referred to conflict mediation. The discipline includes no suspension, no expulsion, and no police involvement. Two Southwestern High School girls are late entering school one morning and are stopped along with numerous other students, handcuffed together, and taken to the Police Department Gang Squad for truancy. The girls are not given a chance to explain why they are late and the final result is a one-day suspension. While these are extreme examples, there does appear to be a lack of clarity and uniformity present in discipline arising from zero tolerance policies.

Zero Tolerance: What is it?

Zero tolerance was intended to create an educational environment in which certain behavior will not be tolerated, punishment will be uniform and students will be able to learn safely [1]. Unfortunately, the effects of zero tolerance have not matched these intentions and instead are detrimental to many students, pushing them out of school and denying them their right to an education [2].

Zero tolerance began in schools as early as 1989, as a term used to explain the mandated expulsion of any student based on violence, drugs or weapons [1]. As the concept was adopted by more schools as a form of discipline, it was adapted to include suspensions and a larger range of offenses including

smoking and school disruption. When the Gun Free Schools Act was passed by the Clinton Administration in 1994, zero tolerance was the key issue. This act mandated that any student caught with a firearm must be expelled for one full school year [1]. Schools that did not comply would lose a portion of their federal funding [3]. But while zero tolerance began as Congress' response to a gun problem in schools, currently the policy is used infrequently to expel students for actual firearms offenses and is widely used for minor infractions [1].

Zero Tolerance in Michigan Public Schools: How do we measure up?

Michigan is one of the most extreme states when it comes to zero tolerance and mandatory expulsions. Michigan has added drugs, alcohol, disobedience, assault, vandalism and verbal threats as offenses that allow for expulsion [3]. During the 1999-2000 academic school year, more than 3,600 students were expelled from Michigan schools in accordance with zero tolerance policies [3]. These policies also create many disparities in the rates at which students are expelled. African-American students are expelled at 2.4 times the rate of other students and Latinos are expelled 1.4 times the rate in comparison to the general student population [3]. The discrepancy transcends race to include gender, as 65% of students expelled are male while males make up just 51.2% of the student population in Michigan. While zero tolerance calls for uniform

punishments, Michigan's statistics force one to consider if other factors play a role in whether students are suspended.

Making Changes—What are people doing to combat zero tolerance issues?

Numerous organizations across the nation are discovering that excluding children from schools is not the answer and are taking action. School districts like the Chicago Public Schools have adapted Peer Juries in their schools, giving students a voice in discipline, to combat the rising numbers of expulsions seen in the school district [4]. Generation Y, the grassroots organization run on Chicago's Southeast side, has been researching the reasons students are pushed out of school, finding that 63% of students were suspended for non-violent, non-drug related behavior, and 30% were suspended for attendance-related behaviors. Youth from this organization desired their voices to be heard and initiated the movement for peer juries.

Sighting a similar problem in their Southwest Detroit community, the youth-led organization, Youth United, is following in this movement for quality education at better schools. The organization has already begun collecting surveys to find out why students are being suspended and is currently working with the Student Advocacy Center in Ann Arbor, MI to find ways to reform the policies that have been pushing them out of their schools.

Conducting Research—The need for more information

Youth United discovered the need for more research through involvement with the community. A comparative study was conducted between the Southwest Detroit schools targeted for change and schools located within the Detroit suburbs that are consistently ranked among the nation's best. A survey designed for students, teachers, and administrators was administered at these school districts concerning discipline procedures and clarity of discipline, school support and atmosphere, and the student's preparation for the future.

The survey and additional interviews were conducted with the objective and hope of gaining a better understanding of the situation in Southwest Detroit by comparing it to other school systems. The key issues pertinent to Southwest Detroit schools and their students needed to be identified in order to be resolved. Unifying themes that pertain to all of

Michigan's public schools are also identified and their resolutions discussed.

Finding #1: Discipline Procedures are Unclear

Through eight one-hour interview sessions with teachers and students from Southwest Detroit, West Bloomfield, MI and Birmingham, MI, it was discovered that discipline procedures are unclear to students and teachers across all three districts, regardless of school ranking or prestige. It appears that while West Bloomfield and Birmingham have clear Codes of Conduct with straightforward rules and accompanying punishments for breaking these rules, students still feel that enforcement of this discipline is neither fair nor uniform. In response to a question concerning how to improve discipline in her school, a Birmingham student felt her school "should be more consistent. They're hypocritical about things and very subjective; they don't treat everyone the same." According to a Chadsey student in Southwest Detroit, "Everyone should have the same rules, some teachers just slack on students. Just because they know that student, the student shouldn't get away with stuff." Students do not perceive discipline as fair and are concerned with administrators' objectivity. Students do not know the disciplinary policy or how and when it will be enforced.

It is here that Southwest Detroit schools lag behind. According to a Southwestern student, "There are just too many people involved in the process—they need someone in charge, not power for everyone. I was suspended by the athletic director who wasn't even there at the time I supposedly did something wrong." When asked the specifics of what happens when you commit certain infractions, Southwest Detroit students replied with varying answers characterized by responses repeatedly including the phrases, "I don't know" and "It depends on the teacher and how they feel."

Finding #2: Students in Southwest Detroit Lack the Support They Need from Their Schools.

As an effect of the preceding finding, students in Southwest Detroit do not feel supported by their schools as compared to students in other school districts. Both the Birmingham and West Bloomfield students claimed to feel very supported by their schools, pointing to policies such as the freedom to start student groups and the many assemblies created to help them as students. Students in Southwest Detroit feel the opposite, with responses such as, "I

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don't think they really care," and "They don't support me at all! They suspend me all the time!" One student from Chadsey felt that the school only supports those felt to be the "good students, the ones they think will succeed, they don't push anyone else, and other students just don't really get the chance." Support by one's school seems to be an indicator of success and a lack of support appears to lead to a student body that is unmotivated to succeed.

Finding #3: Students in Southwest Detroit Feel Their School is not Preparing Them for Their Future.

Lastly, students in Southwest Detroit schools, in comparison with other area schools, do not feel their school is preparing them for their future. As a Southwestern student puts it, "The school isn't preparing me, the school days are just sloppy, some teachers are good, but most just write stuff on the board and tell you, do that." Students in Southwest Detroit do not feel they are offered the classes they need to prepare for or succeed in their futures either, while a Birmingham student can boast, "Yes, we're prepared for our futures, we are a big college prep school."

The Findings—How does it all add up?

Harsh zero tolerance policies appear to be unclear and are not uniformly enforced, leaving students to feel confused and not supported by their schools. Students do not feel they can fight these unfair punishments because of the lack of support. Southwest Detroit students who do not feel their school is preparing them for their futures are at a disadvantage to suburban students who are supported and have college as a goal that is supported fully by the school. Students from both West Bloomfield and Birmingham claimed desires of college were what kept them out of trouble because they did not want their record to have bad marks. Meanwhile Southwest Detroit students fall through the cracks, and as a punishment, they are pushed even farther out of school by disciplinary actions that leave marks on their records, making future options even fewer. Students have a right to be educated, and to obtain the best understanding of the current situation, it is imperative that administrators seek ideas from students to improve the schools.

Recommendations for Better Public Schools in Southwest Detroit

Like Chicago Public Schools, Southwest Detroit needs to implement Peer Juries in their schools to involve students in the disciplinary process and give students a voice and a feeling of control and involvement in their education. However, when approached with this idea, even though students felt excited at the idea of their involvement in discipline, they were again worried that it would not be fair. But according to Jeremy Lahoud the coordinator of Generation Y in Chicago, "Peer juries are important because they put discipline back in the hands of young people, changing the way discipline works. Peer jury is a place where students can go, because even when the rules are clearly spelled out, you get cases sometimes that don't need punishment. Sometimes, punishment just doesn't get at the root issue. You keep enough jurors so you don't have to sit on a jury if it's your friend but really, it's not about the guilt or the innocence. It's not a trial, it's a chance to tell your side, and work to find the solution."

In Conclusion—Listen to the Students

Students need to be involved in disciplinary reforms. The policy and benefit of zero tolerance needs to be clarified and punishments uniformly distributed. Students and the whole community need to be involved in the creation of a better, clearer and more useful code of conduct. This code of conduct then needs to be implemented by the very people who created it—the students—through peer juries. The schools need to be reformed in a manner that will be successful in keeping kids in school, supporting them, involving them, and allowing them to become the successful people they desire to be.

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About the Author

Kelly Alexander is a senior in the Honors Psychology Program at the University of Michigan.

She is currently doing research in Social Psychology on the identity of the self and different roles have and how they effect and impact each other. She is also doing an honors thesis in Clinical and Developmental Psychology, where she conducts interview play sessions with internationally adopted children and codes these sessions to determine the children's attachment strategies. Kelly is interested in pursuing a PhD in School Psychology, and interned with Youth United in Southwest Detroit doing community based research this summer. She plans to keep her research closely related to school and the community, as she finds this to be very important and interesting.



The Role of CD164 in Metastatic Cancer

Aaron M. Havens

J. Wang, Y-X. Sun, G. Heresi, R.S. Taichman

Mentor: Russell Taichman

The spread of tumors, a process called metastasis, is a dreaded complication in the progression of many cancers. This complication is most severe when the tumors spread or 'home' to the bone, as they frequently do in breast or prostate cancers. Blood or hematopoietic cells also 'home' to bone during development and there is now compelling evidence that the growth factor/chemokine (a growth factor that attracts cells) stromal-derived factor-1 (SDF-1) plays a critical major role in the process. We predicted that SDF-1 and its receptor CXCR4, as well as genes activated by SDF-1, may play an essential role in targeting tumors to the bone marrow.

To investigate this hypothesis, we examined prostate cancer as a model for a tumor that frequently metastasizes to bone. Previously, we have demonstrated that prostate cancer cell lines express CXCR4, adhere to endothelium, and migrate through basement membranes in response to SDF-1 [1]. More recently, we determined that SDF-1 and CXCR4 are expressed by human prostate cancers *in vivo* [2]. To identify genes activated by SDF-1 in prostate cancers which might facilitate the establishment of bone metastases, we treated prostate cancers with SDF-1 and examined changes in gene expression at the mRNA level using gene arrays. For our investigations, we treated the metastatic human prostate cancer cell lines LNCaP and LNCaP C4-2B with SDF-1. Originally LNCaP cells were isolated from a lymph node of a patient with widespread bony and lymph node involvement. These cells were passaged in mice until a sub line was identified with increased bone homing capabilities (LNCaP C4-2B) [3]. The LNCaP cells and the LNCaP sub line C4-2B cells were originally obtained from UroCor, Inc (Oklahoma City, OK). Several prostate cancer cell lines were used in our studies.

In order to determine which genes in prostate cancers are altered by treatment with SDF-1, we utilized DNA Microarrays, a tool for the fast monitoring of a large number of genes at once. With

this technology, we analyzed the expression of over 20,000 genes. In general, a microarray consists of gene sequences or fragments of genes called expressed sequence tags (ESTs). Very small amounts of hundreds or thousands of these ESTs are arranged on a single microarray substrate, often glass, usually by a robotic device. The genetic messenger (RNA or mRNA) which signals protein production interest is labeled, purified, and allowed to bind to the microarray. Later an imaging scanner reads the signal intensity (degree of hybridization) of a sample at each spot on the microarray. The analysis software formulates this information generated from the imaging scanner and uses the information to extract, manage and present the information in a usable fashion. In the past, we have only been able to conduct analyses on a few genes at once.

With the development of microarray technology, we can now examine thousands of genes at the same time. In order to perform the microarray analysis, RNA was collected by standard methods from SDF-1 stimulated LNCaP and LNCaP C4-2B cells and compared to RNA collected from cells that were not treated with SDF-1. For our analysis, we used 4 Affymetrix HG-U133A chips that contained signals for approximately one half of the human genome, obtained by the University of Michigan Dental School Microarray Facility. The raw data was transferred into the statistical software and then calculated expression values were performed using a Robust Multi-array Average (RMA).[4]. We chose this program to 'fit' a model to the data in order to calculate relative expression values [5]. After the expression values were calculated, the data was further analyzed using Significance Analysis of Microarrays (SAM), a program that calculates various statistical tests with adjustments for multiple comparisons using False Discovery Rate (FDR) [6]. The comparison of the SDF-1 (at a physiologic dose of 200 ng/ml) treated and untreated cells was straightforward and performed using a t-test that

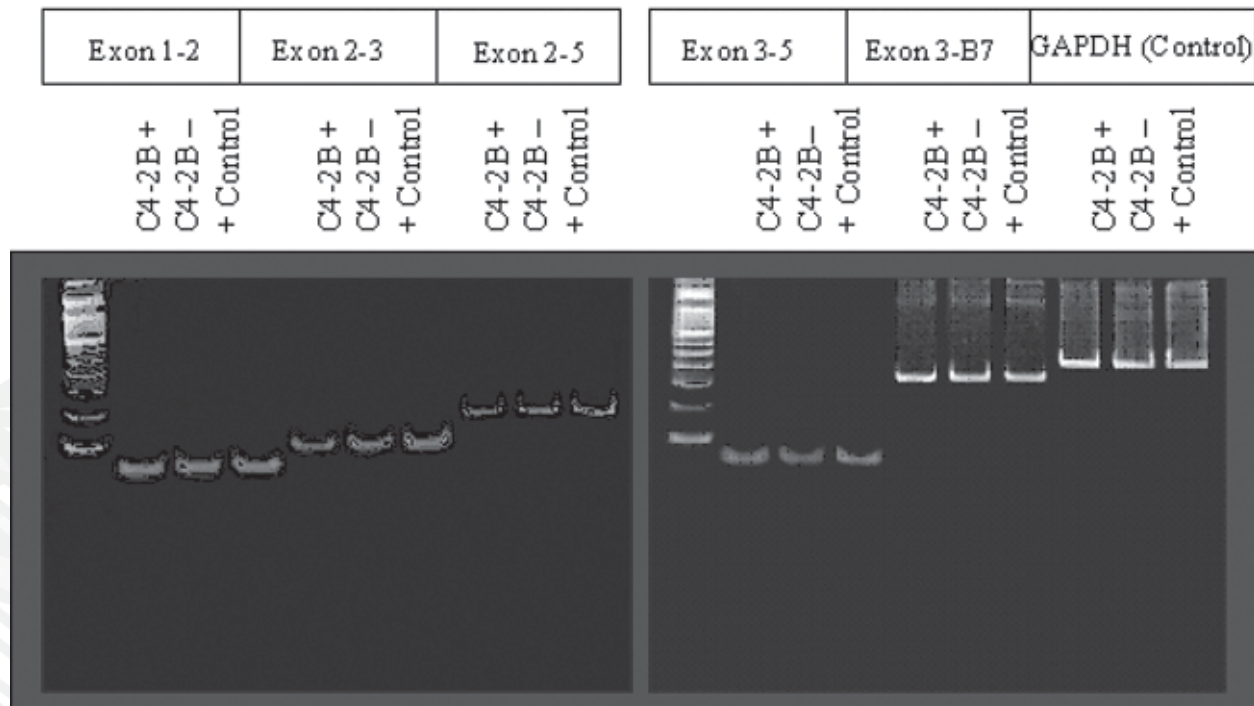


Figure 1: Gel Electrophoresis of CD164 Exon 1-6 This non-quantitative polyacrylamide gel shows the DNA sequences depicted over the designated exons (coding regions of DNA). Three types of cDNA are shown for each set of primers (probes for detecting the presence of the DNA) presented. Data is for LNCaP C4-2B cells treated with SDF-1(+), or cells that were not treated (-). The human hematopoietic cell line KG1a was utilized as a positive control. A molecular weight ladder corresponding to differences in 100 base pairs is shown to the left of each figure.

compares the mean of the expression values for each gene (at each time).

Initially our analysis revealed that there were ~300 genes in which expression increased in response to SDF-1. From these, the gene CD164 was identified as a SDF-1-responsive gene that is potentially involved in the homing process of prostate cancers to the marrow. CD164 is a protein of ~160 kDa initially identified on very primitive blood cell precursors. CD164 is known to function as an adhesion receptor during blood development, facilitating the adhesion of these early cells to their support cells in the bone marrow (or stromal cells) [7,8].

To verify the results from the microarray, we examined several prostate cancer cells for the expression of CD164 by Reverse Transcriptase – Polymerase Chain Reaction (RT-PCR). This technology was first developed in the late 1980's and allows one to rapidly assess the presence or absence of a gene in a given sample of messenger RNA. We chose reagents for these analyses that were designed

to cross intron/exon boundaries to ensure that we were not obtaining false positive signals. The first step in this technology was to isolate mRNA from the cells of interest and to then convert the mRNA into a complementary copy of DNA. Polymerase Chain Reaction or PCR was then used to make many copies of the gene CD164, and we incorporated many controls into our experiment to control for false signals. The PCR product was then analyzed in a DNA or polyacrylamide gel, where the amount of DNA base pairs can be quantified. As illustrated in Figure 1, gel electrophoresis shows that CD164 is expressed by the bone homing prostate cancer cell line LNCaP C4-2B, and the major mRNA produced by the tumor cells is the full length version of the mRNA (unspliced species). We cloned and sequenced the RT-PCR product to confirm this result. (Figure 2). The RT-PCR result provided further validation of the microarray results.

In order to determine whether prostate cancer cells actually make the protein coded for by the mRNA

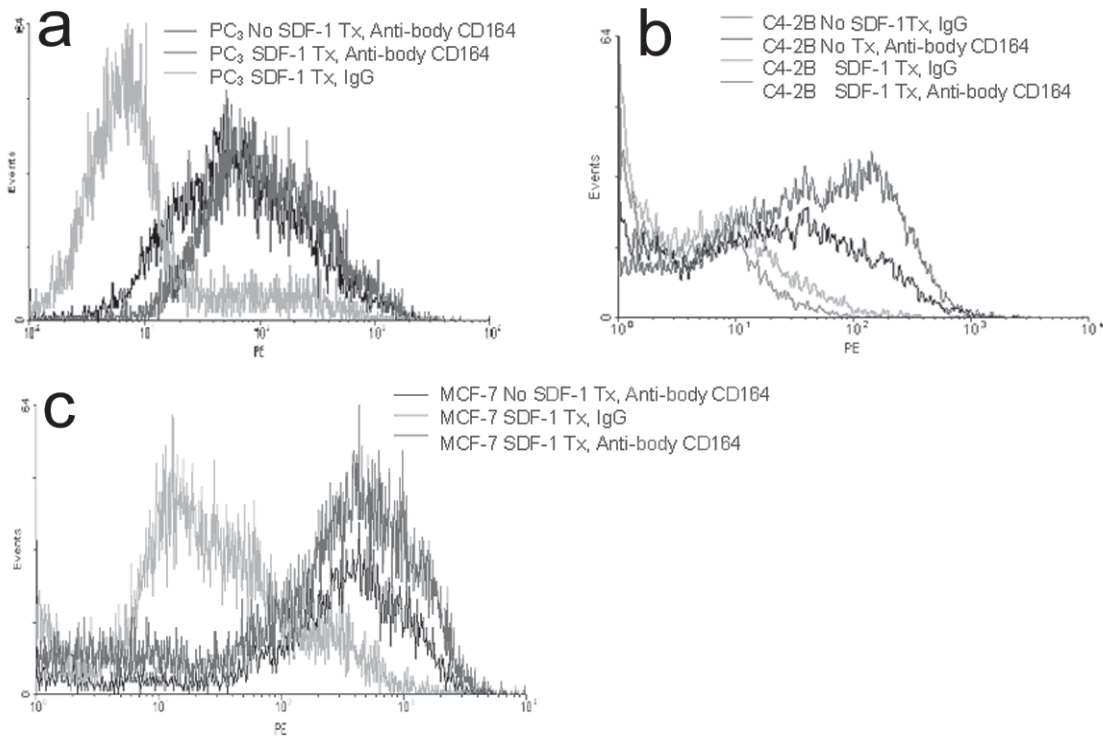


Figure 3: Flow Cytometry Analysis for SDF-1 Stimulated PC3 or LNCaP C4-2B Cells A.) Flow cytometry results of PC₃ cells treated with SDF-1. The slight shift of the antibody-stained cells of SDF-1 treatment for 3 hours shows that more PC₃ cells were stained during analysis. B.) Flow cytometry results of LNCaP C4-2B cells treated with SDF-1. The shift of the antibody-stained cells with SDF-1 treatment for 2 hours shows that the expression of CD164 is increased as the levels of SDF-1 are heightened when compared to the antibody-stained cells with no SDF-1 treatment. C.) Flow Cytometry results of MCF-7 cells treated with SDF-1. Both graphs show an IgG control.

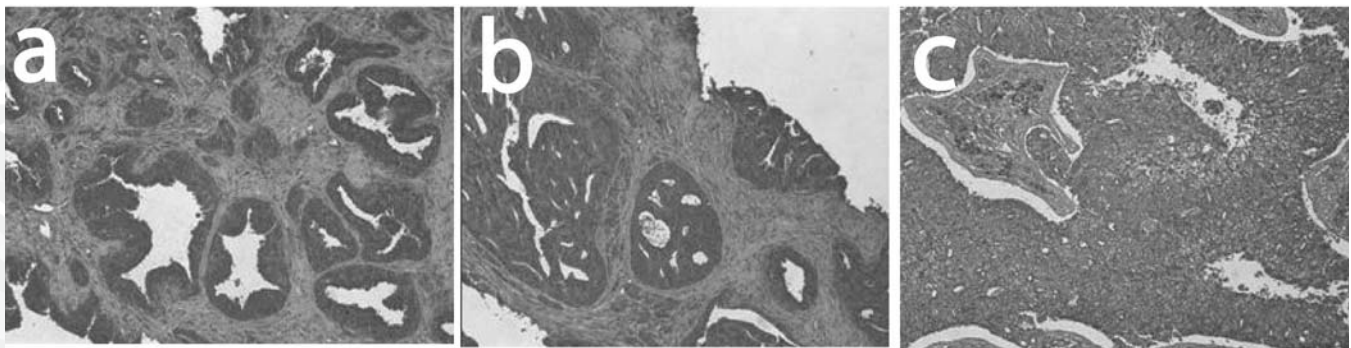


Figure 4: Immunohistochemistry of Prostate Cancer and Lymph Node

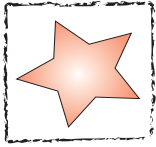
Immunohistochemistry was performed on patient samples of both prostate cancer and lymph node cells. The samples were stained with an antibody to CD164. (A, B) Human prostate cancer tissue biopsy demonstrated the intense brown staining of CD164, indicating the presence of CD164 in human prostate cancer. (20X) (C.) Positive control staining of a human lymph node at 20x magnification.

the ability of the enzyme to break down a substrate that turns a color – the result in this case is the presence of a brown stain on the tissue samples (Figure 4). The data demonstrates that CD164 is expressed by prostate cancer cells in patients and is not merely related to a culture artifact.

In summary, we have identified CD164 as a SDF-1 responsive gene in prostate cancers that is a reasonable candidate for a protein possibly involved in homing to the bone marrow. Thus far we have determined that CD164 mRNA is expressed by prostate cancer cell lines in relation to SDF-1 treatment. In addition, we have determined the protein expression of CD164 through flow cytometry or FACs analysis of metastatic cancer cell lines. At this point we have also found that the gene CD164 is responsive to heightened levels of SDF-1 and believe that CD164 is a gene responsible for adhesion molecules involved in prostate cancer homing to the bone marrow. Further studies are underway to determine the relative expression of CD164 in a large number of human samples relative to tumor aggressiveness. These preliminary studies may ultimately lead better targeted therapy to prevent prostate cancer metastasis.

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Individual Child Variability Upon Entrance Into Preschool

Lisa Slominski

Mentor: Carol Connor, Fred Morrison

Over the past decade, research has supported what teachers and parents have known intuitively for years: children's academic skills are highly variable. Throughout the elementary school years and within a single age group, there are almost always some children who can read simple books while others do not know the letters of the alphabet; there are some children who can add and subtract while others cannot count to ten; and there are some children who thrive academically while others fall behind. This gap in academic successes becomes even more pronounced in later school years, and can, potentially, affect the types of academic and career paths that an individual will follow throughout his or her life. Yet while the existence of individual differences in academic skills among children is indisputable, the question remains as to when these individual differences begin in life, and what they can tell us about the importance of the school and home environments to the cognitive and social development of children.

When researchers first began to address these questions, the focus tended to be on older children who were performing at varying academic levels. In recent years, however, researchers have begun to turn their attention to younger children in an attempt to discover at what age the variability in important academic skills begins to appear. In the past decade there have been a number of studies that have discovered individual differences in children's academic skills when children first enter kindergarten [1,2]. Even in kindergarten, some children possess high levels of vital academic skills whereas others do not. This is an important finding because it suggests that individual differences in academic achievements appear earlier in life than had been previously thought, and indicates that the environmental influences a child encounters before entering kindergarten are important to the child's later academic success.

Researchers also began to recognize the importance of early academic skills for later academic achievement [3]. Studies have found that academic skills in early elementary school can predict some

aspects of children's performance, such as how well a child reads, throughout the rest of their school years. Researchers have found, for example, that a child's relative academic standing remains reasonably stable from around third grade through high school [4]. This means that a child who is performing poorly academically in third grade will most likely perform poorly academically in high school. In other words, if a child does not learn important academic skills early on, perhaps even by the time he or she is in kindergarten, that child has a higher chance of falling behind later in his or her academic career.

All of these studies led to a focus on the search for early predictors of academic skills in children. What is it about one child that makes him or her succeed in school, while another child does not? Although some differences in cognitive ability can be attributed to differences within the child, such as I.Q. or biological factors, increasing evidence suggests that the early experiences a child has at home and at preschool should be considered sources of potential influence [5]. Potential predictors such as ethnicity, gender, family literacy environment, maternal education, and months in child care centers have all been examined in children as early as kindergarten to try to find associations between these factors and academic performance [6]. These studies found, as expected, that what happened in a child's home before he or she started school (for example, how often the parent read to the child at home) seemed to affect how well the child would do in school for years to come.

But when do these differences in academic abilities really begin to appear? Could the individual differences present in kindergarten and early elementary school be attributed to the fact that some children had attended preschool while others had not? Would a group of children who had never had previous formal schooling experiences still show significant variability in academic skills? In other words, what are the nature and sources of individual differences before a child starts school?

This study sought to answer some of these questions, and focused on children entering preschool. Two hundred one preschool children with an average age of four years participated in this study; all were recruited from six public preschool programs within a Michigan school district. As a group, the children could be described as a typical population of preschool children within the United States. Demographically, the children were mainly from middle to upper-middle class families, and identified with a variety of ethnic and religious groups. The majority of children also came from families with moderately high socioeconomic standings. One might expect this large population of young, same-aged children from similar social backgrounds to perform similarly on tests of cognitive abilities. One goal of this study was to determine if this was true.

In order to test this assumption, the study children had to be assessed early in the school year. Within the first few months of their initial entry into a public preschool program, the 201 children in this study were given two 40-minute batteries of assessments. One assessment instrument used was the Woodcock-Johnson III Tests of Achievement [7]. The tests within the Woodcock-Johnson III measure basic skills that have been found to predict academic achievement in elementary school. The assessments analyzed in the present study included: 1) Letter-Word Identification, which measures word identification skills; 2) Applied Problems, which measures analytical and mathematical skills; 3) Picture Vocabulary, which measures word knowledge; and 4) Academic Knowledge, which measures the extent of basic academic information a child has acquired. The second assessment instrument used was the Test of Early Language Development (TELD). This assessment battery contains a Receptive Test, which is designed to measure components of early language, such as listening skills and reading comprehension, and an Expressive Test, which measures skills such as meaningful speech generation. The assessments utilized were designed to determine and describe the status of a child's academic strengths and weaknesses, and allowed researchers to make comparisons between individual children.

For the purposes of the present study, the 201 preschool children were split into two groups that will be referred to as "young preschoolers" and "old preschoolers". The groups were split on the basis of the formal cut-off date that the school district set as a requirement for entry into its public preschool

programs. Children in this Michigan school district must be at least 2 years 11 months old to enter preschool, and any child 2 years 10 months or younger when school begins must wait until the next year. For this study, the children were split into two groups: the first group (the young preschoolers) was composed of the children who had been too young to enter into preschool the previous year, and the second group (the old preschoolers) was made up of those children old enough to have attended preschool the previous year. As a result, many of the old preschoolers were entering their second year of preschool, while all of the young preschoolers were entering the public preschool program for the first time. At the time of testing, the young preschoolers group consisted of 83 children, ages 3 years 10 months and younger, and the old preschoolers group consisted of 118 children, ages 3 years 11 months and older. The average age of the young preschoolers was 3.44 years, and the average age of the old preschoolers was 4.33 years. The intent of this division was to examine the importance of schooling in the very early years. All of the children were close in age, separated only by an arbitrary cut-off date set by the school district. Would the children who might have had an extra year of preschool perform better on tests of academic achievement, or is preschool not as integral to academic development as the later school years have proven to be? Would variability in academic skills be present within the two groups, as well as between them?

To help answer these questions, the scores that the children in this study received on the four Woodcock-Johnson III tests and the two TELD tests were analyzed and compared. In order to make the results easy to compare, each child's raw scores on the assessments were first converted into age-equivalent scores. Age-equivalent scores were calculated based on the average scores of a large representative sample of an age group in the entire population of the United States. For example, an age-equivalent score of 4 years 3 months means that a child has scored at the level of an average 4-year-3-month-old child in the United States. Since all of the children in this study were approximately 4 years old, the age-equivalent scores can be used to assess how well the study children were doing in comparison to a representative sample of other children in the United States. These scores also give a clear picture of the variability present in a sample, and illustrate the range that a group of scores spans.

TELD Receptive Score Age Equivalency Distribution for Preschoolers

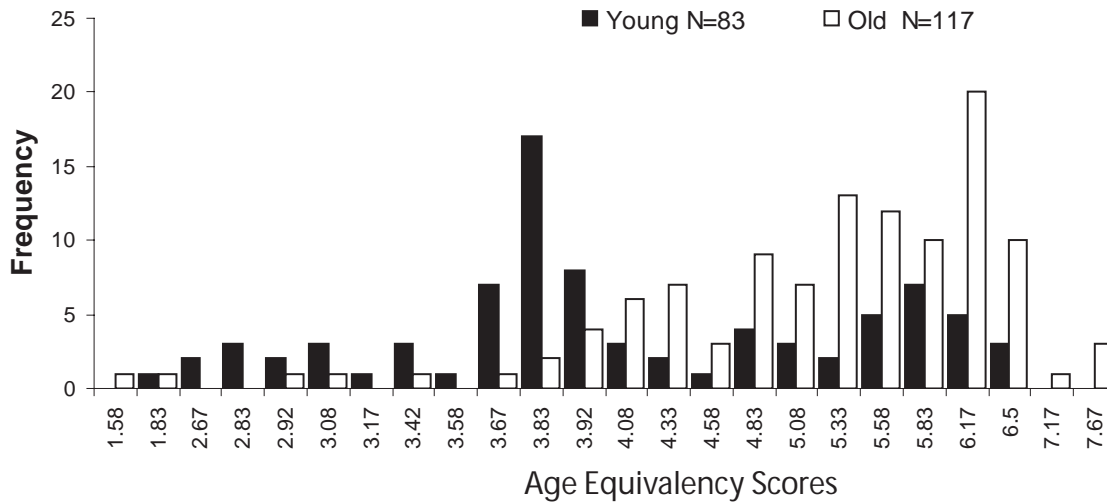


Figure 1

This figure displays the range and distribution of preschoolers' scores on the TELD Receptive Test. Age equivalency scores were computed from raw scores, and based on the average scores obtained by a large representative sample in the United States. Both young and old preschoolers in this sample displayed a wide range of variability in their age equivalency scores, with old preschoolers achieving higher scores overall.

Woodcock-Johnson III Picture Vocabulary Age Equivalency Distribution for Preschoolers

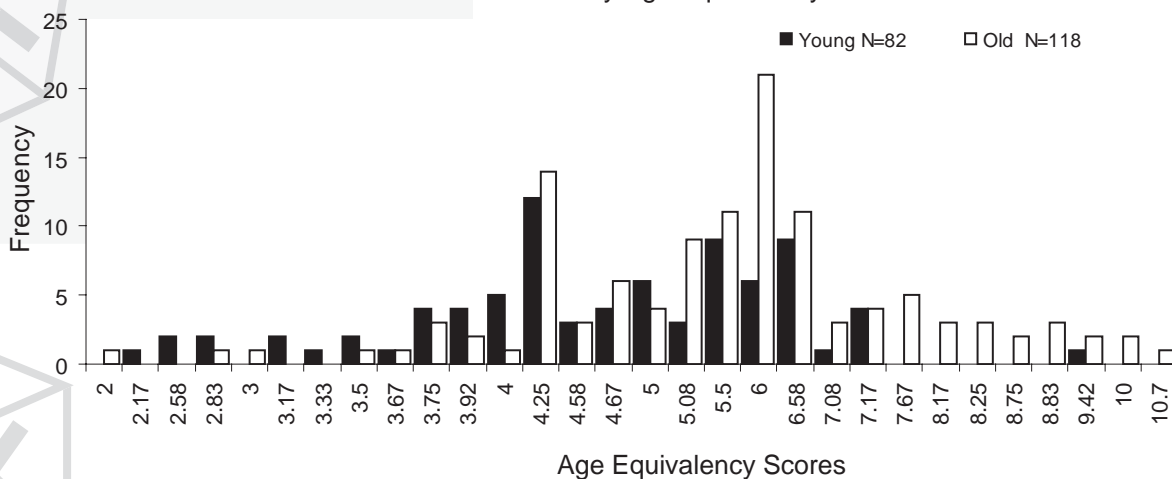


Figure 2

This figure displays the range and distribution of preschoolers' scores on the Woodcock-Johnson III Picture Vocabulary Test. Age equivalency scores were computed from raw scores, and based on the average scores obtained by a large representative sample in the United States. Both young and old preschoolers in this sample displayed a wide range of variability in their age equivalency scores, with old preschoolers achieving higher scores overall.

The results of this study show that children enter preschool with widely varying levels of academic skills in all areas (See Figures 1 and 2). When examining the age-equivalent scores of both the young and old preschoolers, it is apparent that, while many children's scores cluster between 3 and 5 years, there is a great deal of variability within this range, and also outside of it. In almost all of the tests, there were some children who obtained scores equivalent to that of average one or two-year-olds, and others who obtained scores equivalent to that of six-, seven-, or eight-year-olds. In one test, the TELD Receptive Test, two children scored at an age-equivalency of 1 year 10 months, while two others of approximately the same age scored at an age-equivalency of 8 years 2 months on the same test (Figure 1). In the Woodcock-Johnson III Picture Vocabulary Test, one old preschooler achieved an age-equivalent score of 2 years 10 months, while another old preschooler achieved an age-equivalent score of 10 years 8 months (Figure 2). Similar variability occurred in each of the other tests.

Notably, even though the young preschoolers were too young to have entered a public preschool program prior to the year of testing, these children still showed a great deal of variability in their academic competencies (See Figure 1 and 2). This is important because it removes previous preschool experience as a possible source of variability in this group. In other words, since the children in this group were too young to have attended preschool before, and since they still showed vast individual differences in academic skills, then other experiences during the children's first few years of life, such as home or day care experiences, can be regarded as significant sources of variability in academic skills when the children first enter preschool.

Some differences also existed between the groups of young and old preschoolers. As expected, the old preschoolers achieved higher average age-equivalent scores than the young preschoolers on all six tests that were administered. The difference between the average age-equivalent score of the young preschoolers and the average age-equivalent score of the old preschoolers was 9 months for the Letter Word and Picture Vocabulary Tests, 11 months for the Applied Problems and TELD Expressive Tests, 12 months for the Academic Knowledge Test, and 13 months for the TELD Receptive Test (See Table 1). While some of the difference between young and old preschoolers' test scores can be attributed to

the fact that the old preschoolers were slightly older than the young preschoolers, prior preschool experience must also be considered as an influence. Previous studies have shown that the number of years spent in preschool is related to achievement test scores in later grades; children who had more years of preschool scored higher on various tests of academic skills [8]. The present study supports this finding, because the previous schooling experience of the old preschoolers most likely contributed to the higher average scores that they achieved.

The results of this study highlight the importance of both early home experiences and early preschool experiences to the development of crucial academic skills. In all of the academic areas tested and throughout the entire span of ages that the preschoolers represented, a high degree of variability was present. In every test, some of the children scored as low as toddlers would, while others scored as high as fifth or sixth graders. The fact that all of these children were approximately the same age, from relatively similar backgrounds, and attending the same preschools indicates that other factors, such as early home environment and parenting practices, should be considered important predictors of academic abilities in children as young as 3 years old. Early experiences in a preschool classroom were also found to be important, and this study signifies that an extra year of preschool may contribute to higher scores on tests of academic achievement.

Since academic proficiency in the early years has been found to predict academic success in later years, the fact that a child enters preschool with relatively weaker academic skills can also potentially affect and predict how well the child will do academically in elementary school, high school, and beyond. The results of this study indicate the importance of both the early home environment and early preschool experiences to the development of academic abilities. Future studies will focus on both of these areas in order to elucidate the home and schooling factors, and their complex interactions, that shape children's development of crucial early academic skills. Hopefully, this study has set the foundation for future work exploring ways in which to help those children who lag behind in school early on, so they do not remain behind for the rest of their school years.

Average Age-Equivalent Scores for Young and Old Preschoolers

TEST	CUT-OFF GROUP	MEAN AGE-EQUIVALENT SCORES
Letter Word	Young Preschoolers	4 yrs. 5 mo.
	Old Preschoolers	5 yrs. 2 mo.
Applied Problems	Young Preschoolers	4 yrs. 1 mo.
	Old Preschoolers	5 yrs. 0 mo.
Picture Vocabulary	Young Preschoolers	5 yrs. 0 mo.
	Old Preschoolers	5 yrs. 9 mo.
Academic Knowledge	Young Preschoolers	4 yrs. 2 mo.
	Old Preschoolers	5 yrs. 2 mo.
TELD Receptive	Young Preschoolers	4 yrs. 4 mo.
	Old Preschoolers	5 yrs. 5 mo.
TELD Expressive	Young Preschoolers	3 yrs. 9 mo.
	Old Preschoolers	4 yrs. 8 mo.

Table 1: This table displays the mean age-equivalent scores for both young and old preschoolers on the six different assessments that were given to children upon entering preschool. The old preschoolers obtained higher mean age-equivalent scores than the young preschoolers did on all tests administered.

Acknowledgements

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About the Author

Lisa Slominski is a third year undergraduate in psychology and anthropology at the University of Michigan. She participated in the Undergraduate Research Opportunity Program her sophomore year, and worked in the Pathways to Literacy lab in the department of psychology. She continues to work in the lab under the guidance of Dr. Fred Morrison and Dr. Carol Connor.



The Effect of Wheel Training on Cognition Following Unilateral Entorhinal Cortex Injury

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Mentor: Alice E. Davis

Traumatic brain injury (TBI) adversely affects an individual's memory, learning, and orientation. It is hypothesized that damage to the entorhinal cortex (EC) will lead to loss of sensory integration and cognitive dysfunction. Not all TBIs are symmetrical throughout the brain. If a car is sideswiped in a motor vehicle collision the sideways motion could cause the driver to hit their head on one side only. The impact could cause brain damage to the immediate area or damage to the other lobe. Damage to only one side of the brain could lead to different losses of cognitive and behavioral recovery. The loss of sensory integration, which is intimately tied to memory and learning, necessitates more study. The purpose of this study was to research the effect of wheel training on cognition following unilateral entorhinal cortex injury.

Sensory integration is the process of sorting external stimuli, such as vision, sound, smell, and touch, into discernible signals through the different levels of the brain. For example, a dog that first hears a rabbit in the grass turns to look at the rabbit and receives a visual stimulus of the rabbit that enhances the original sound. A blind dog would have a harder time locating the rabbit using only sound. Multisensory pathways integrate environment stimuli from different parts of the brain in order to form a memory or a motor response. In this process, the EC (located in the middle temporal lobe between the hippocampus (HPC) and the sibiliculum) is used in conjunction with the HPC and dentate gyrus to integrate external stimuli [1].

Survivors with TBI continue to receive multiple stimulations from their environment, but often have difficulty integrating these stimuli to form memories. In 1994, Zola-Morgan related hippocampal damage to the severity of memory impairment and found that injuries to both HPC and EC showed a marked increase in memory impairment over HPC injuries alone. These results show that the EC is used in conjunction with the HPC for memory [1].

Background and Significance

The outside environment creates a multitude of simultaneous stimuli. The multisensory pathways that exist throughout the EC help to process these stimuli for the HPC. Information from the EC is then sent to various receptive fields in the brain according to the origin of the stimulation. The receptive fields then integrate the information and form the reaction and memory of the situation. Multiple stimulations in a normal brain excite these receptive fields within the HPC [2]. After injury, the presence of differentiated stimuli can lead to repression of the receptive fields due to missing integrating pathways. This repression will lead to difficulty forming new memories and controlling reactions in an intensely stimulated environment. For example, if a subject is unable to integrate or process multiple stimulations simultaneously, an overload will occur, because different receptive fields will be firing different signals [2]. If, for example, one noise occurs to the left while another occurs to the right, but if the subject is incapable of integrating the information, both stimulations would be depressed and neither would be acknowledged.

Every day people use multiple sensory stimuli to form memories. For a certain sound, a particular picture is brought to mind. This association is created through a process that involves the EC. The EC helps process information from sensory inputs to the HPC. Lavenex shows that the EC is not merely a relay of multisensory information to the hippocampus, but participates actively in the memory processes by further integrating information [3].

The HPC is associated with long and short-term memory. Different stimuli received from the secondary integration pathways of the EC help create both the long and short-term memory [3]. When the EC is injured, the paths of sensory integration to the HPC and memory formation are disrupted. Loesche

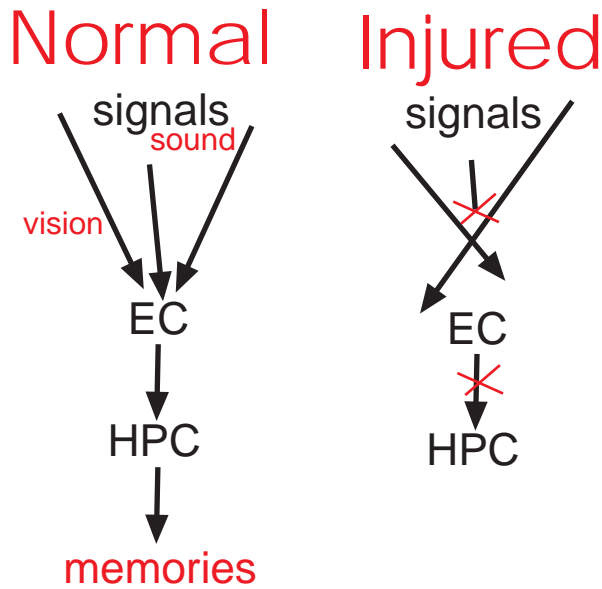


Figure 1

and Steward and Davis et al (2000) demonstrated this disruption through the deficit in the training and cognition of their bilateral and unilateral EC injured animals.

According to Loesche and Steward [4], subjects with unilateral EC damage were able to improve cognitive performance with time because of rewiring of the EC through the dentate gyrus. Specifically, Loesche and Steward hypothesized that cells in the dentate gyrus were reinnervated in part by nerve cell axons from the central lateral EC. This process, when the remaining uninjured neurons reconnect pathways, is known as plasticity. Although plasticity occurs after EC lesions, the degree of functional return is limited and is dependent on the difficulty or demand of a task [5]. A simple task may not require the animal to develop many projections of the EC into the dentate gyrus, but a more complex task can stimulate additional growth necessary for the animal to perform satisfactorily. For unilateral EC lesions, animals can partially reinnervate back into the dentate gyrus [5] so that complex motor stimulation

of these animals should be able to increase the performance standard set by Loesche and Steward.

High frequencies of unilateral injuries necessitate plasticity of the injured area to help restore cognitive function. The specific aim of this study was to determine if a high demand, complex task wheel training would improve cognitive function in animals with unilateral EC injury. The hypothesis tested was that the wheel task helps increase the cognitive performance of the unilateral EC injury animals in a swimming maze.

Design

Experiments measured indicators of unilateral EC injury and cognition by varying the complexity of the wheel task. Research lasted 21 days with animals from the University of Michigan labs. A reverse 12-hour light-dark cycle was used so animals were at peak activity during testing and surgery. The animals were given four days to adjust to the new cycle before injury. Control and injured animals were selected randomly on day four. After injury, the animals were given two days of rest. After the two-day rest, the injured animals were again randomly divided into a continuous (group B) or intermittent wheel group (group A). The intermittent wheel group would run the first and last day of the 12 days of testing and the continuous group had six days of consecutive testing followed by six days of rest and retraining on day 12. Wheel testing started on the 4th day post-operation and continued until the 15th day post-operation. Each day the animals completed one round of testing (Fig. 2). After wheel testing, all animals were tested for cognition six days using a water maze over a period of six days.

Surgical Procedure

Unilateral lesions were created in the rats using specifically placed electrically pulsed leads as described by Loesche and Steward [4]. Post

Group	Test 1	Test 2	Test 3	Test 4	Test 5	Test 6	Test12
A	✓						✓
B	✓	✓	✓	✓	✓	✓	✓

Figure 2 : Wheel Training Schedule

experiment brains were removed and sliced horizontally in 80-micron sections. Brain slices were stained with cresyl violet and analyzed for extent and location of injury under a light microscope according to the parameter set forth in Paxinos [6].

Behavioral Testing – Three days following EC damage animals were tested using a wheel task [7]. The purpose of this task was to implement sensory integration and motor training for the animals. The motor task of the wheel helps to develop a sensitization to maintaining balance on the wheel and a habituation of wheel walking [7]. The number of times the wheel task was used depended on an animal’s group. The wheel task consisted of one-minute total interval training where demand changes, from simple to complex, were made by increasing the speed of the wheel. A simple wheel task was to walk on top of a wheel that switched directions every 15 seconds. To remain on the wheel, animals had to learn to turn. The wheel task was a measure of sensory integration that to require that required the animals to use multiple senses including vision, hearing, balance, vestibule-motor, etc [7]. The wheel started slowly and increased its speed per certain number of trials. A complex wheel task built on the simple wheel task by increasing sensory stimuli. These sensory inputs included olfactory, visual, balance, and tactile stimuli used simultaneously.

Following the 12 days of wheel training, a swim task was used to measure the effects of the motor training upon cognitive orientation. The water maze was chosen as a reliable measure of spatial learning. The water maze was a 5-foot diameter by 3-foot deep pool. The water was shaded white with dry powdered milk to hide the white platform just

barely beneath the water level. This platform was placed at the same location every day with cues around the pool, also in the same location every day. Animals were dropped at different locations around the pool and their swim paths, exploratory behaviors, and swim times recorded (Davis, 2001).

Twenty days from the injury, a probe memory test was conducted to see if the animals had learned the location of the platform after completing water maze training (Davis, 2001). For the probe test, the platform was removed completely from the pool. The animals were dropped into the water and allowed to explore the tub for 30 seconds. The path of exploration, including initial heading direction, was taken after the animal had been dropped into the water. Following the probe trial, cue tests were run to see if the animals could learn to swim towards a cued platform rather than the previously learned submerged platform. Cue tests consisted of removing the platform from the usual location and placing a novel platform with a visual cue in another location in the tub. The animals were dropped and their path, time, and exploratory behaviors were recorded just as in the water maze test in the 2001 Davis study [8].

Sample

The animals were Sprague-Dawley male rats. These animals were chosen specifically due to their increased ability to survive after lesion surgery, and because human males receive TBI 4:1 over human females.

Results

HISTOLOGY– Lesions produced damage to the entire medial and lateral EC. Animals with lesions

	n	Mean	SD
Uni B	6	33.1	57.2
Uni A	5	56.4	62.4
Con B	11	34.9	53.7
Con A	14	30	51.9

Table 1: Probe Directional Heading Error

Uni B = unilaterally injured with continual wheel training

Uni A = unilaterally injured with intermittent wheel training

Con B = control with continual wheel training

Con A = control with intermittent wheel training

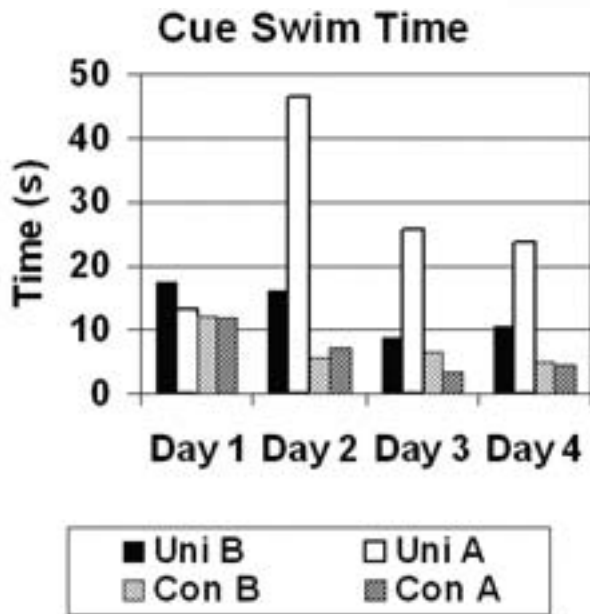


Figure 3

in the thalamus, superior colliculus, or cerebellum were eliminated from analysis, leaving 36 total animals. Lesions could not have damaged more than 20% of the hippocampus and more than 10% of the midbrain, thalamus, and basal ganglia. The minimum extent of damage and maximum to either side are available for comparison.

PROBE DIRECTIONAL HEADING ERROR: Unilaterally injured animals without wheel training had increased mean directional heading error in the probe task compared to controls with and without wheel training (Table 1). Unilaterally injured animals with wheel training had a mean heading error comparable to that of controls with and without wheel training. Error was greater than chance in these animals compared to injured animals with training and all controls. Overall, controls had no significant

difference in mean heading error. Below, n is sample group size and SD is standard deviation for each mean.

CUE SWIM TIME EC: Injured animals and controls look similar on the first trial because all were unfamiliar with the task (Table 2). On trial 2 injured animals without wheel training took almost 9 times longer than controls and 3 times longer than injured animals with training to reach the cue. This trend continued in the animals without training, but gap diminished during the third and fourth trials. The between group effect in the injured groups was not significant ($p = .075$). Significance is $p < .05$. P values are statistical ways of showing significance in data, so the lower the number, the more significant the results are. No between group effect was found for controls

Discussion

In this study, animals with unilateral EC lesions exposed to a 7-day wheel-training task had improved cognitive function compared to animals without a 7-day wheel-training program. These results support the hypothesis that a wheel task helps increase the cognitive performance of the unilateral EC injury animals in the swimming maze. The results in this study also support the recommendations of Loesche and Steward [4], who set up a timeline for the cognitive recovery of unilateral EC injury. They suggested that modifying a post lesion testing/retraining program could improve performance and possibly shorten recovery time. Their hypothesis was tested in this experiment and the conclusions are: 1. Wheel training enhanced memory in animals with unilateral injury to the entorhinal cortex during a probe trial. 2. Wheel training enhanced learning in animals with unilateral injury to the entorhinal cortex during a cue trial. 3. Wheel training did not influence memory or learning in control animals. 4. A planned sensory stimulation and motor

Group	n	Mean 1 (SD)	Mean 2 (SD)	Mean 3 (SD)	Mean 4 (SD)	p
Uni B	6	17.3s(18.3s)	16s(16.5s)	8.8s(5.5s)	10.5s(7.5s)	.075
Uni A	5	13.2s(9.5s)	46.6s(51.1s)	25.8s(17.1s)	23.8s(25.6s)	
Control B	11	12.0s(6.8s)	5.5s(3.7s)	6.5s(3.2s)	5.1s(3.0s)	.859
Control A	14	11.8s(7.1s)	7.1s(3.3s)	6.2s(2.7s)	4.6s(2.0s)	

Table 2: Cue Swim Time

activity program influenced cognitive recovery from unilateral entorhinal cortex injury.

It is possible that the improvement comes from undamaged EC being forced to integrate several stimuli, thus increasing demand for multisensory integration through the EC. The more intense pattern of firing can help retrain the brain to use new pathways or create them through the damaged EC. Repression or excitement of the receptive fields of the animal may eventually have adjusted to the stimuli, integrating multisensory information through the injured EC. These are possible reasons for the development improved memory and learning after the wheel task.

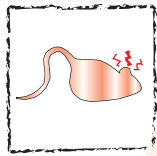
Conclusion

The results provide some evidence that a post lesion retraining program may improve overall cognitive performance in unilaterally EC injured animals when compared to each other. Significance may not have been reached because this was a side study using accidental unilaterals. Future studies in this area should involve examining histological changes related to plasticity. The site and extent of plasticity needs to be examined and documented. Also, in this study there is no differentiation between left or right EC unilaterally injured animals. Therefore, planned use of unilateral injury to examine these same trends needs to include differences between left and right EC injury. Future studies could provide further information for increasing the cognitive performance of unilaterally injured animals by changing the post-training task. Eventually, a post lesion-retraining program to improve overall cognition in TBI humans may be developed.

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Role of the Posterior Paraventricular Thalamus in HPA Axis Function and Habituation

Kavita Bhavsar

Mentor: Seema Bhatnagar

The main objective of our project was to gain a better understanding of the effects of chronic stress upon the Hypothalamic-Pituitary-Adrenal (HPA) Axis. Stress in this context may be defined as any threat to homeostasis, or internal environmental balance, of the body [1]. It is important to distinguish the effect of chronic and acute stress upon HPA axis function. Stress can be short-term (acute) or long-term (chronic). Acute stress is the reaction to an immediate threat and is commonly known as the “fight or flight” response [1]. The threat can be any situation that is experienced as a danger. Common stressors include noise, crowding, isolation, illness, hunger, danger and infection. Such stress signals cause the sympathetic nervous system to increase blood pressure and temperature along with adrenalin levels [2].

In contrast, chronic stress includes ongoing disturbances such as psychological pressures, loneliness, physical illness, and financial worries. The consequences of acute stress upon HPA axis activity have been widely studied through many diverse experiments. However, detailed information regarding

the function of the HPA axis during periods of chronic stress is still lacking. Further, chronic stress has been associated with specific disorders such as depression and post-traumatic stress disorder [1]. It has been found that HPA axis performance is disrupted during depression; the adrenal gland is considerably enlarged and many patients exhibit high levels of cortisol in the blood stream [3]. Further, excessive levels of corticosteroids over a protracted period are damaging to the immune and nervous systems. In addition, it is interesting to note that aging can be associated with a series of events that excessively stimulate the HPA system while simultaneously weakening the strength of negative feedback responses which terminate corticosteroid generation [4]. Therefore, our study of high levels of chronic stress in the brains of lab rats is extremely significant.

Since chronic stressors have been observed to change the response characteristics of the HPA axis [5], it is crucial to understand how the system works. If the system is operating optimally, there is a prompt shutdown of the HPA axis at the termination

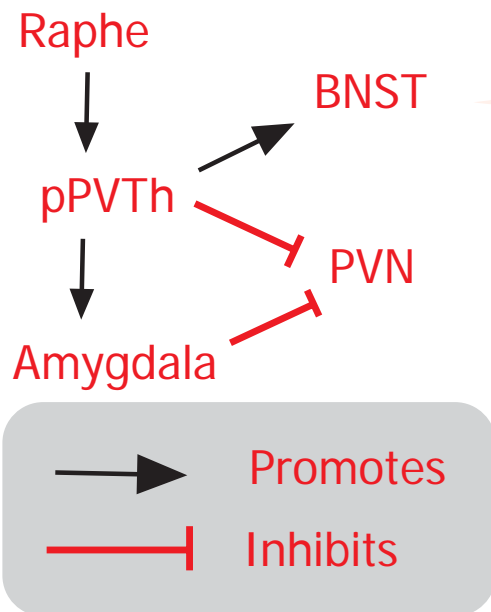


Figure 1: Stress Neuronal Circuit The figure above shows possible pathways through which the pPVTh works in order to affect the PVN and ultimately the response to stress. It is believed that the pPVTh functions by inhibiting the amygdala, which normally acts to stimulate the PVN. However, the pPVTh may work through other extensions as well in addition to its output to the amygdala. The pPVTh may directly send an output to the PVN, or may extend to the BNST. The inhibitory effect on the PVN may be achieved by the amygdala working through the BNST to reach the PVN instead of directly extending to the PVN. The raphe nucleus and its secretion of serotonin may also have some important implications.

Mice Number and Type	Stress Type and Trial #	Staining Results
7 (DH2) Mice- with sham lesions	Chronic- Trial 1	All mice exhibited little staining
12 (DH2) Mice- with actual lesions	Chronic- Trial 1	10/12 mice exhibited heavy staining
6 (DH3) Mice- with sham lesions	Acute- Trial 1	All mice exhibited little staining
14 (DH3) Mice- with actual lesions	Acute- Trial 1	14/15 mice exhibited little staining

Table 1: Animals in the study group DH2 were chronically stressed only. DH2 animals underwent sham and pPVTh lesioning. DH3 animals, however, were only acutely stressed, but also underwent both types of lesioning.

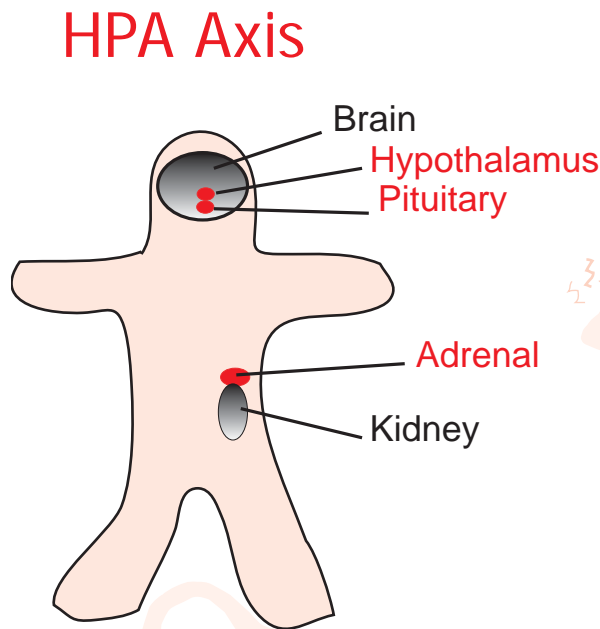


Figure 2: Hypothalamic-Pituitary-Adrenal Axis The HPA Axis is a complex network of feedback inhibition utilizing corticosteroids.

of a stress signal. This indicates that the HPA axis behaves as a negative feedback system. It also appears to be the major brain pathway regulating neuroendocrine, autonomic, and immune responses to shifts in homeostasis as a result of stress [6]. The HPA axis ultimately regulates stress responses through the management of glucocorticoid secretion in the outer layer of the adrenal gland, or the adrenal cortex [3]. These manufactured corticosteroids are essential throughout the body in order to promote the conversion of proteins and lipids to carbohydrates, but in the context of stress, they serve as signals of negative feedback [5].

Upon close inspection, it is evident that the HPA axis consists of a complex arrangement of particular nuclei and neuronal structures which act in synchrony (Figure 2). Stress signals trigger the Paraventricular Hypothalamic Nucleus (PVN), which

in turn mediates secretion of the proteins Corticotropin-releasing Hormone (CRH) and Arginine Vasopressin [4]. These proteins potentiate the production of another ‘messenger’ substance termed Adrenocorticotropin (ACTH), which acts upon the receptors in the adrenal cortex, increasing the secretion of glucocorticoids (corticosterone or cortisol) released into the bloodstream [7]. Corticosteroids serve as signals of negative feedback because an increase in levels of cortisol and corticosterone leads to decreased synthesis of ACTH.

Next, our particular study investigates in particular the function of the Paraventricular Thalamus (pPVTh) in the HPA axis. Data obtained from previous studies has shown that pPVTh lesions enhance facilitation of stress response and lesions of this area block habituation. The pPVTh is thought to function, more importantly, only at the onset of chronic stress. Our research continued this line of study by examining which brain regions are changed by pPVTh lesions in acute vs. chronically stressed rats. It was hypothesized that the pPVTh functions to inhibit the PVN directly or through various neuronal circuits involving the pPVTh (Figure 1). The pPVTh receives input from the dorsal raphe and sends an output to the basolateral, basomedial, and central nuclei of the Amygdala which also extends to the PVN. The dorsal raphe is a key brain structure which is responsible for the production of the pleasure-stimulating neurotransmitter, serotonin. The amygdala similarly controls emotions, but covers a broad range of feelings including anger and fear. It is believed that the pPVTh normally functions to inhibit the amygdala, which acts to stimulate the PVN and hence stress response. However, the pPVTh may also extend to the bed nucleus of the stria terminalis (BNST), which contains central and medial extended amygdala elements (Figure 1).

In our animal studies, we utilized Sprague-Dawley male rats. Our first study was randomly termed DH2. In this study, seven rats were sham lesioned and twelve rats underwent actual pPVTh lesions. Sham lesions are superficial lesions and were

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performed for both the DH2 and DH3 studies in order to ensure that the results obtained were due to the actual destruction of the tissue, not the process of delving into the brain. Both DH2 sham and pPVTh lesioned animals were chronically stressed by being placed in restraint cages for thirty minute intervals per day over a period of seven days. On day eight, the animals were euthanized and after one hour the brains were perfused.

The DH3 study, in contrast, utilized acute stressors. Six rats were sham lesioned and fourteen rats underwent pPVTh lesions. The 20 rats were placed in restraint cages for thirty minutes on day one, and euthanized (also on day one). Following death, the rat brains were perfused in parallel to the DH2 study.

Next, brains obtained from both DH2 and DH3 studies were surgically removed and preserved in formalin so that they could be sliced. Brains were sliced at 30 microns. These slices of brain tissue then underwent a staining procedure coined Fos-Immunocytochemistry (Fos ICC), in which the protein secretions of activated neurons are visually marked. Following Fos ICC, each slice of tissue was mounted on a slide, and the slides were analyzed under a high power microscope to evaluate which brain regions were activated during stress.

It was anticipated that the HPA axis would be highly activated and exhibit heavy Fos staining when the pPVTh was lesioned in chronically stressed rats only. Acutely stressed rats with pPVTh lesions were expected to exhibit less Fos staining than chronically stressed rats with pPVTh lesions. Moreover, acutely stressed rats with pPVTh and sham lesions were expected to show equivalent amounts of Fos staining. Sham lesioning of chronically stressed rats should have no effect on normal HPA axis operation, and the inhibitory role of the pPVTh should remain functional and undisrupted. Thus, chronically stressed rats with sham lesions were also expected to show little Fos staining. Specific brain regions that were expected to show activation during the chronic stressing of the pPVTh lesioned animals included the amygdala, BNST, and the PVN.

Preliminary results indicate that only pPVTh lesioned animals exhibited high Fos staining during chronic stressing, implying that the normal function of the pPVTh is indeed to inhibit the PVN.

Future studies will continue this line of research by lesioning areas other than the pPVTh, such as the amygdala and the BNST. If the amygdala

is destroyed, will the pPVTh still be able to function normally through the BNST or a direct extension to the PVN? Or is the amygdala necessary for the inhibitory effect of the pPVTh on the PVN? More research is necessary to clarify the pathways of response to chronic stress.

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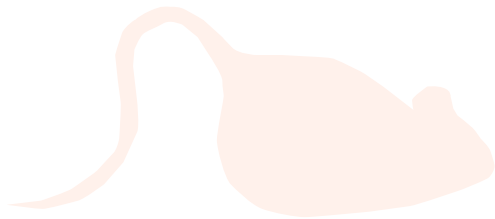
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The ICC and the Transatlantic Conflict

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Introduction

The International Criminal Court (ICC), the first transnational legal body, has its roots in the 'Rome Statute', signed on July 1, 1998. It is intended to hold individuals accountable for the four core crimes of genocide, war crimes, crimes against humanity, and the crime of aggression. To take effect, the ICC treaty needed to be ratified by at least 60 states; despite the strong objection of the current U.S. Administration, this number was reached in April 2002. Shortly before, the Bush Administration had announced that it did not intend to ratify the Statute, and moreover, that it considered itself as released from any obligation arising from the American signature of the Rome Statute, given by former President Bill Clinton on December 31, 2000. This withdrawal, unique in the history of international relations, provoked harsh criticism in the international community and from the member states of the European Union in particular.

The fundamental gap between the European and American position on the ICC issue has greatly aggravated transatlantic conflict. The main difference between the two positions involves the question of whether 'Universal Human Rights Jurisdiction' constitutes an infringement on American national sovereignty. Within this issue, the debate centers on prosecutorial powers, the question of immunity, the risk of politically motivated prosecutions and the rights of the accused in trial procedures. Each of these topics will be explored in this analysis.

Underlying the ICC case is a transatlantic clash of ideologies centering on two fundamentally different interpretations of national sovereignty. Whereas the European Union considers the ICC as an expansion of its national sovereignty and its sphere of influence, the U.S. views it as an infringement on its constitutional rights (Macpherson & Kaufman, 2002, p. 220). The EU fears a possible 'double standard' in international human rights law if U.S. citizens would be granted unconditional immunity,

while the U.S. on the contrary opposes 'automatism' in ICC jurisdiction as a result of its universality.

Prosecutorial Powers

A major concern of U.S. officials since the beginning of the Court negotiations in 1994 has been the ICC prosecutor's ability to check state decision-making in order to prevent states from committing genocide or crimes against humanity (Washburn, 2002). As the investigations can start without a referral from either the UN Security Council or a state, opponents to the ICC assumed that the prosecutor could attempt to influence domestic policy-making and violate sovereignty rights (Macpherson & Kaufman, 2002). Therefore the U.S. sought guarantees that only the UN Security Council should have the power to start investigations, because such rights in the hands of a "less-than-impartial prosecutor" (Macpherson & Kaufman, 2002, p. 220) would not be compatible with American constitutional safeguards. The appointment of ICC judges through nomination by the Assembly of States was also criticized, since these nominations could be politically motivated. The American delegation to the Rome Conference stressed that the ICC prosecutor's "ability [...] to bypass the Security Council would undermine the settled system of international governance and the U.S. role in that system" (Amann, 2002, p. 3). This American argument was based on Articles 7[1] and 24[1] of the Charter of the United Nations, which guarantee the SC the "primary responsibility for the maintenance of international peace and security" (Amann, 2002, p. 3). Currently, the United States plays a key role within the Security Council, as it is one of the five permanent members with the right for absolute veto. The ICC is, in this view, a threat to that primacy.

The European response to the American fear of excessive prosecutorial power was to point to the safeguards and checks and balances implemented in the Rome Statute itself. The "unaccountable prosecutor" (Bolton, 2002, p. 2) was, in the eyes of the EU negotiators, no more than a theoretical worst-

case scenario. They argued that “the investigations of the ICC prosecutor can be stopped by a vote of two judges within the ICC’s Pre-Trial-Chamber” (Amann, 2002, p. 4). Furthermore, the accused state itself has “the right to challenge the jurisdiction of the Court and its admissibility of a case” (Lee, 2002, p. 3). John Washburn points out in support for this position that the limits for the ICC prosecutor are tight. “It can determine only whether an act was in fact pursuant to a particular plan or policy”(Washburn, 2002, p. 2).

Regarding the American fear of politically motivated nominations of ICC prosecutors, the EU took the standpoint that the US was consciously overemphasizing that “non-democratic state parties” (Amann, 2002, p. 4) could try to use the institutional framework of the ICC as an arena for their hostile actions. The EU stressed that the large majority of the member states of the Assembly of States are stable democracies which have excellent relations with the US. Historical precedence and the record of international institutions like the UN give no evidence of scenarios like the ‘unaccountable prosecutor’.

As to the US fear that the ICC is a challenge to the primacy of the Security Council, the EU emphasized the central role of the UN SC under the present ICC Statute (Macpherson & Kaufman, 2002). Article 13(b) rules that referrals made by the Security Council must be accepted by the ICC prosecutor, if all permanent members and a majority of the nonpermanent members of the SC agree upon them. Lee emphasizes that the right of referral can even be used as an instrument for the Security Council in managing future international crises: the ICC can replace the costly and time-consuming ad hoc tribunals set up by the SC such as those in Yugoslavia and Rwanda (Lee, 2002). The obvious ineffectiveness of the ad hoc tribunals to cope with mass atrocities like the Rwanda Genocide, Lee argues, make the call for a permanent law enforcement mechanism even more urgent. “Eight years after the genocide and six years after prosecutions at both national and international level, more than ninety-five percent of the prisoners are still waiting for trials in overcrowded detention centers”(Lee, 2002, p. 8). A permanent institution like the ICC would, to a large extent, solve the problem of ineffective Security Council tribunals. This claim can be based upon the higher degree of effectiveness of permanent legal bodies compared with ad hoc institutions which have to struggle with high transaction costs every time they are set up. Moreover, the affinity of the permanent institution is considerably higher.

Furthermore, the “Singapore Compromise” (Sewall, 2000, p. 63), a last minute attempt to mediate between the US and the EU positions in this problem, suggested that the American request for a subordination of the ICC under the authority of the Security Council could be transformed into the right for the UN body to delay ICC investigations and initiate a commission to examine the legitimacy of the ICC measures. Article 16 of the current Statute gives the Security Council “a form of collective control” (Macpherson & Kaufman, 2002, p. 221), confirming that the permanent members of the SC have the right to “postpone an investigation for up to 12 months on a renewable basis” (Macpherson & Kaufman, 2002, p. 221).

The Question of Immunity

The U.S. also insisted that existing international treaty law prohibits the ICC from exercising jurisdiction over nationals of states which have not ratified the Rome Statute, including the U.S. (Sewall, 2000). American head delegate David Scheffer told the Senate, “the treaty purports to establish an arrangement whereby U.S. armed forces operating overseas could be conceivably prosecuted by the international court, even if the United States has not agreed to be bound by the treaty” (Sewall, 2000, p.214). This argument is a direct challenge of the principle of universality as established in the Rome Statute. US Opponents to the ICC call this universality a ‘jurisdictional overreach’, and argue that two problems arise from it.

First, the Rome Statute incorporates crimes that are not recognized as crimes of universal jurisdiction under customary international law, particularly the as yet undefined core crime of ‘Aggression’ (Macpherson & Kaufman, 2002). Second, according to the US, universal jurisdiction cannot be subject to a treaty-based collective international court. Legitimacy for US overseas action derives only from domestic sources like “the United States’ constitutional structures and democratic principles” (Patrick and Forman, 2002, p.47), never from a treaty-based collective. The American understanding of state sovereignty in this respect is one of unilateral universal jurisdiction, that is, “a State has jurisdiction to unilaterally prescribe, adjudicate and enforce laws. This amounts to firstly establishing its laws with regards to persons, secondly applying these laws to these persons in criminal proceedings and finally inducing or compelling compliance or punishing

non-compliance with these laws” (Strapatas, 2002, p. 2). These rights cannot be delegated to international bodies.

Proponents of the Court like Bickley mark these American arguments as weak. He notes that an implementation of the US conditions in the ICC Statute would “prevent the prosecution of Saddam Hussein for War Crimes committed by his forces in Kuwait unless he consented” (Macpherson & Kaufman, 2002, p. 223). Other scholars highlight that the American stance runs counter to the US self-created precedent regarding several international crime definitions, like terrorism and hijacking.

Yet one important weakness in the arguments of the European Union regarding the question of immunity remains: the question of the as yet undefined crime of aggression.

Crime of Aggression - The risk of politically motivated prosecutions

US ‘Under Secretary for Arms Control and International Security’ John R. Bolton calls the definition of aggression “excessively elastic” (Bolton, 2002, p. 2). The ICC could become a “political forum” (Sewall, 2000, p. 213) to challenge political decisions from high US officials, and non-democratic states may initiate politicized prosecutions. As member states of the ICC are represented in the Assembly of States under the principle of ‘One Nation - One Vote’, the likelihood of such scenarios is seen in Washington as very realistic.

The American argument against a criminal definition of aggression is often referred to as the ‘exceptionalist debate,’ meaning that the US deserves exceptional treatment because of its unique role in international peacekeeping operations. The US fears that preemptive military actions such as the air strike on the Al Shiffa pharmaceutical plant in Sudan will be interpreted as aggression. After the US attacked the plant in Sudan on August 20, 1998, “the president of Sudan called for international prosecution of the U.S. officials behind the air strike” (Sewall, 2000, p. 213). He labeled the air strike a crime of aggression and war crime. Because of fears that US service members could be prosecuted for similar operations, the US wanted the “right of veto to prevent any of its own nationals being brought to trial” (Macpherson & Kaufman, 2002, p. 221).

However, the EU refused to grant the US veto power, stating that the crimes under ICC jurisdiction were crimes against humanity, which

deserve treatment as absolute universal crimes. The EU pointed out that exemptions were counter-productive to the goals of the ICC and would set a dangerous example undermining the authority of the Court.

There are several views concerning the current debate over the crime of aggression. Some argue that this Crime will never be defined, because of its sensitivity and the lack of consensus for a common definition under the ICC Statute. And there are those, like Dr. Claus Kress (Kress, 2002), who maintain that, based on customary international law, aggression will be regarded as the type of war initiated by Hitler. There is no evidence, according to Kress, that military actions of type ‘Kosovo 1999’ or ‘Afghanistan 2001’ could ever be included into the crime definition of aggression, especially considering the national interests of the large majority of the Assembly of States. As a definition of the Crime of Aggression has to be adopted with a two-thirds majority within this body, Kress sees the US concerns to a certain extent devitalized (Kress, 2002).

Regarding politically motivated prosecutions initiated not by a hostile state party but by a biased prosecutor, Amann adds that under the principle of complementarity, the ICC judges cannot approach a case as long as a national jurisdiction is “willing” to precede it. Some ICC supporters, such as Amnesty International, claim that the United States would ensure its national interests if it would enact national human rights legislation identical or similar to the ICC jurisdiction into the American Constitution, because the more “US laws conform to those of the ICC, the more the US legal system can deal with cases that might interest the ICC, and thus shield US nationals from international prosecution” (Amann, 2002, p. 10).]

The rights of the accused in trial procedures

Some American law experts see in the ICC Statute the risk of unfair trial proceedings, because it lacks fundamental U.S. constitutional safeguards such as the right to trial by jury and protection against double jeopardy. Also missing are alternatives to prosecution. The US argues that the failure of the ICC to “acknowledge the legitimacy of local amnesties,” which are a tool of truth commissions, cannot be accepted (Macpherson & Kaufman, 2002, p 222-24). But this standpoint is not universal in America. One representative of the American Bar Association announced in a congressional hearing that the “Treaty of Rome contains the most comprehensive list of due

process protections which has so far been promulgated” (Amann, 2002, p.5).

There is also no reason why the lack of a right to trial by jury necessarily precludes US participation in an ICC court. Numerous examples in US legal practice show that there is already variance permitted in the rules of procedure. American military courts are not restricted to the guidelines of the civilian procedures, and furthermore, the US has historically cooperated with international military tribunals, even when procedural differences existed. “US courts also have rejected US nationals’ claims that the Constitution forbids their surrender to foreign courts that follow procedures unlike those in the United States” (Amann, 2002, p. 10). These examples suggest that “as long as the ICC’s practices meet minimum standards of fairness, they should not prevent US participation in the international court” (Amann, 2002, p.11). Additionally, Article 53 of the Rome Statute vests the ICC prosecutor with the power to decline a case, where “a prosecution is not in the interests of justice, taking into account all circumstances” (Macpherson & Kaufman, 2002, p 224), which may be interpreted as allowing the ICC to grant or recognize amnesties.

Conclusion

The US position on the ICC Statute claims that it violates certain aspects of the American constitution, mainly concerning prosecutorial powers, immunity, the risk of politically motivated prosecutions and the rights of the accused in trial procedures. However, these objections are based on a basic ideological rift between the US and the European countries over the idea of state sovereignty.

The US definition of state sovereignty is based only on domestic legitimization, while the EU definition includes also the delegation of sovereign rights to international legal bodies. The US understanding is best described with the words of John Marshall, former chief of Justice of the United States, who said: “The jurisdiction of the nation, within its own territory, is necessarily exclusive and absolute ...” (Amann, 2002, p. 9). This implicates that “no International Court has the right to override US law in the trial of US citizen” (Macpherson & Kaufman, 2002, p. 220). The EU definition of state sovereignty is shaped by a ‘dualism’ between supranational jurisdiction and legislature, and intergovernmental national decision-making. This was proven in the negotiations on the ICC, when all member states of the European Union

adhered to a definition of state sovereignty grounded on Absolute Universal Jurisdiction.

Necessary policy steps

The following policy recommendations which would improve the situation pragmatically are taking for granted that both sides, even in times of extraordinary transatlantic tensions have a natural interest to continue to cooperate. This assumption stays valid even in case of ideological and conceptual disagreement like we have seen in the ICC dispute. However, all pragmatic steps will have to focus first on improving the transatlantic relationship in general, especially since the open confrontation about the Iraq war in 2003 has destroyed several channels of mutual understanding. Reinvention of effective transatlantic communication on the basis of “lowest-common-denominator policy” (Moravcsik, 2003, p.81) is therefore crucial. Moravcsik suggests striking a new “Transatlantic Bargain”. As in most of its history, the Western Alliance should again clearly distinguish between core cooperation and other, controversial issues. Informal issue-related work summits could help in this respect moving beyond superficial accusations on both sides. An early warning system for crisis management centering in something like a ‘Transatlantic Council’ could produce decent diplomatic agreement or at least understanding before both sides battle their problems in the media.

After a revitalization of the transatlantic communication channels, both the US and the EU must take several steps to promote an atmosphere of mutual trust. This will demand concessions on both sides. First, the US should amend its US Federal Criminal Code (Title 18) and the Uniform Code of Military Justice (Title 10) to ensure that they incorporate all ICC-defined crimes. This would demonstrate the commitment of the US to the fight for international human rights and, secondly, ensure that all possible ICC crimes could be investigated domestically under the principle of complementarity. Additionally, the US should limit its claims for immunity to the as yet undefined crime of aggression, and cease its efforts to pressure governments into Article 98(2) International Agreements, which is a bilateral agreement between the US and any foreign government that US citizens will not be surrendered to ICC jurisdiction under any circumstances. This agreement is unreasonable when ICC jurisdiction covers the worst crimes against humanity, and undermines the position of the US in its insistence on

immunity in the case of aggression. Only Americans under the guidance of the US government, such as soldiers and diplomats, should gain immunity. Finally, states making bilateral agreements with the US should be excluded from the right to protect their national citizens before the ICC, meaning that EU member states must restrict themselves from demanding exemptions. The EU on the other hand should engage in dialogue with Washington about the crime of aggression. A work-summit could introduce a new formula for a crime definition, which would not hinder the US to engage into preemptive invasions if they are clearly marked by their humanitarian intention and backed by the international community. If no compromise can be reached, EU officials should promote an exclusion of this crime definition from the Rome Statute. In this way, Washington could rethink its position to join. Moreover, the EU should encourage the newly elected 1st ICC prosecutor, Argentine lawyer Luis Moreno Ocampo, to engage in intense dialogue with Washington, in the hope to destroy the idea of the 'unaccountable prosecutor'. In particular, the courts' principles of complementarity with national legislation can play a crucial role to convince Washington that as long as American legal institutions are engaged in investigations, the ICC will not take over jurisdiction.

The ICC is as much an example of an ideological rift as it is a conceptual rift between the European Union and the United States of America. The 'new realism' in US foreign policy since September 11th will constantly overlap with and confront the EU's attempt to transfer its own framework of binding multilateral agreements onto the level of the international community. Therefore we have some evidence that the key problems we have seen in the case of the ICC (such as the definition of state sovereignty) will also hinder or even block necessary coordinated policy steps in the future. A new Transatlantic bargain, as suggested by Moravcsik, should therefore focus rather on viable and institutionalized conflict management than on continuing to evoke the spirit of shared transatlantic values.

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