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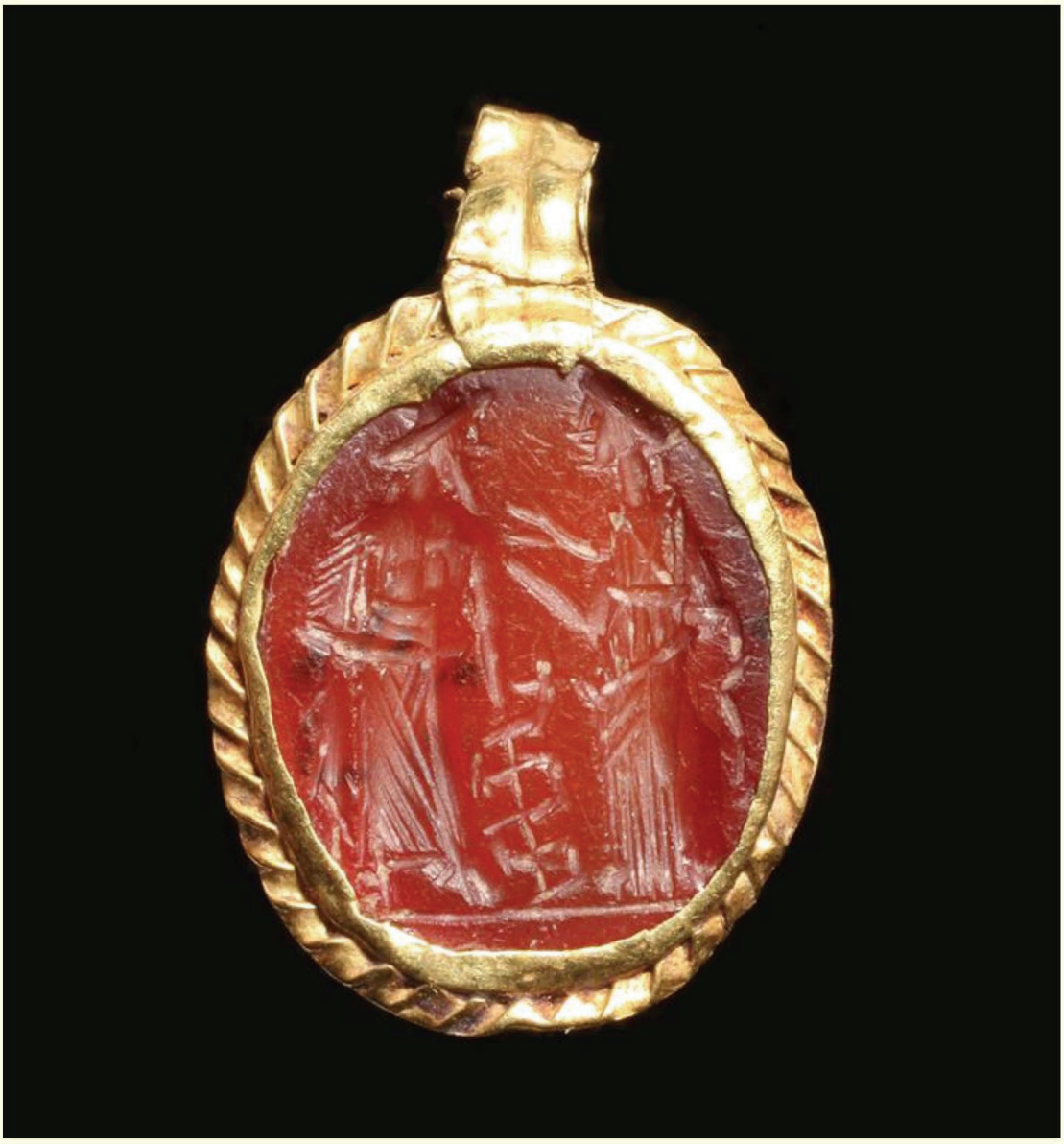

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Editorial Leadership

University of Missouri-Columbia
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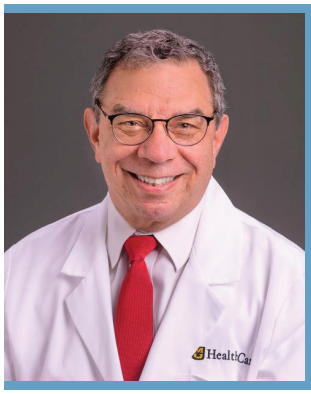

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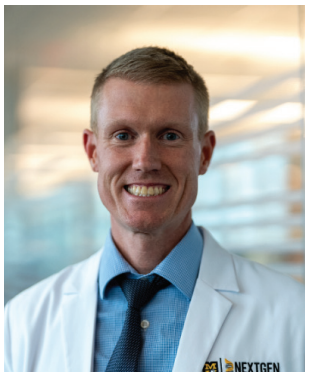

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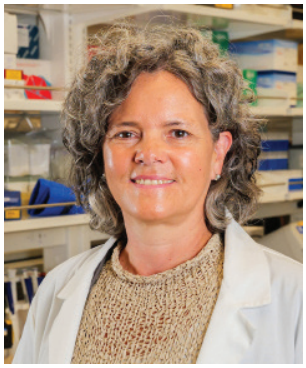

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Marie Nau Hunter

Interim Director
Museum of Art and Archaeology, University of Missouri

On front: Pendant with Asclepius and Hygieia (suspension loop missing), Roman, 3rd–4th century CE, gold and carnelian, Weinberg Fund (85.52).

Museum records on the pendant selected as the cover image for this issue of Missouri Health provide basic context about the scene:

The healing god Asclepius is shown here with his daughter, Hygieia. He holds his snake-entwined staff with the head of the serpent between them. To wear such a pendant was probably thought to bring the owner good health.

The ancient Greek god Asclepius is one who should be of interest to readers of Missouri Health. Perhaps the most significant son of Apollo, Asclepius was associated with a variety of healing practices and locations and was esteemed for his ability to cure the sick. His five daughters were also linked with themes of good health or recuperation. The daughter depicted on the museum's pendant is the goddess Hygieia whose name is the source for the term "hygiene." Sometimes called the rod of Asclepius, the staff included in the scene appears similar to the caduceus, a well-known and long-time symbol of medicine.

The scene of Asclepius and Hygieia is engraved into a gemstone, a method called "intaglio." This technique allows the object to be used like a stamp when pressed into a soft material like wax or wet clay. The carved images are then shown in reverse. Intaglio seals would have functioned as a form of ancient signature that could confirm the identity of the owner.

Pictured: impression of the scene

The pendant is currently on view in our Weinberg Gallery of Antiquities, named for the modern-day founders of the museum, Saul S. and Gladys D. Weinberg, both of whom were field archaeologists. The Weinbergs are both deceased, but their support of our mission continues via an endowment fund they established to assist with acquisitions, like the pendant pictured, and research focused on the ancient world.

We hope you'll make time to visit the Museum of Art and Archaeology to see the pendant and the many other works included in our galleries. The museum is located in the heart of campus, in the lower east side of Ellis Library, with entrances off Hitt Street, Lowry Mall, and from within Ellis. It is just a short walk from the Mizzou Medical School and University and Children's Hospitals. Our regular weekday hours are 10 a.m. to 4 p.m. Tuesday through Friday, and noon to 4 p.m. on Saturdays and Sundays. Admission to the museum is always free.

We are grateful that Missouri Health editors continue to partner with the museum to provide cover images for this publication. It affords us the important opportunity to introduce new audiences to the museum.

For more information about the Museum of Art and Archaeology, including a calendar of events and a searchable database of the museum's permanent collection, visit maa.missouri.edu.

Letter from the Founding Editor

By Richard J. Barohn, MD

Founding Editor, Missouri Health
Executive Vice Chancellor for Health Affairs
Hugh E. and Sarah D. Stephenson Dean, MU School of Medicine

I am happy that we are publishing Volume 3/ Issue 1 of Missouri Health. This is a major breakthrough issue because it is the first Missouri Health that has peer reviewed articles from our students, residents and faculty. We plan to have this as an ongoing feature of each issue. I encourage you to continue to send in manuscripts to Missouri Health. They can be manuscripts that emanate from an abstract presented at a research event on campus that may have been previously published in the journal. Or it may be information that has not been presented at a campus research day.

In this issue there is an interesting case report and of the use of cenobamate for seizures in pregnancy from the neurology department. Another case report with a literature review is from the dermatology department describes how venous stasis dermatitis can be a risk factor for bacteremia from Pasteurella multocida. The students and faculty from the orthopedic department have two manuscripts. One is a very nice retrospective study of over 700 patients undergoing spine surgery at MUHC. They showed that if postoperative physical therapy is initiated on postoperative day 0 rather than postoperative day 1 this resulted in a lower hospital length of stay. The other manuscript analyzed patients who underwent proximal femur fracture fixation and showed the mortality rate was not impacted by the patients rural residential status.

We also are publishing he abstracts form the 2025 Ellis Fischel Cancer Center research day and the Nextgen Precision health pathways research day. I hope some of these presentations are submitted to Missouri Health as full length articles.

Also in this issue we are publishing a number of speeches that were given this year. I am publishing remarks I gave at three different events. I was asked to speak at the annual University of Missouri Library Society and Legacy Society annual reception in Ellis Library. This was a thrill for me to do and was able to talk about the importance of libraries and books in my life. When I was asked to give welcoming remarks to first year medical students and then incoming PhD students I discussed many of the potential career pathways they can pursue with their MD and PhD degrees. I think the

comments and the accompanying career opportunity diagrams will be of use to physician and scientist students in the early phases of their careers.

Dr Lauren Umstattd MD , SOM class of 2015, gave a wonderful speech at this years commencement event for our graduating physicians. In her comments she provided what she referred to as a “new playbook” of advice to the graduates The five areas of advice on which she focused were : 1) Protect Yourself; 2) Choose Yourself First; 3) Be Loud When They Want you Silent; and 4) Build the Career You Actually Want; and 5) Learn the Game- Then Play It Your Way. It was an exciting and motivational speech and I asked Dr Umstattd if we could publish it in Missouri Health. I am very glad she agreed.

Finally, the student editors again chose the art for the cover of Missouri Health from the extraordinary collection in the University of Missouri’s Museum of Art and Archaeology. They chose a pendant Roman from 3rd to 4th century that pictures Asclepius the god of healing in ancient Roman civilization. Interim museum director Marie Nau Hunter again was kind enough to provide information about this beautiful piece of art, and once again encourages all of the Missouri Health readers to visit the museum in the ground floor of the Ellis Library.

In November we had another busy and large research day. Those abstracts will be published in the spring/summer issue of Missouri Health. We will have a number of full length articles in that issue as well.

Richard J. Barohn, MD
Executive Vice Chancellor for Health Affairs / Hugh E. and Sarah D. Stephenson
Dean, School of Medicine

Comments made at the University of Missouri library society and legacy society annual reception
University of Missouri School of Medicine
April 25, 2025

Comments by Richard J. Barohn, MD
Executive Vice Chancellor for Health Affairs Hugh E. and Sarah D. Stephenson Dean, MU School of Medicine

Thank you so much for inviting me to join you today.
My name is Rick Barohn, and I am the executive vice chancellor for health affairs and dean of the School of Medicine.

I am a true librobibliomaniac. And that is not a word in the Oxford English Dictionary (OED). Bibliomania is in the OED.[1] I looked it up in my 20-volume OED that I have at home this morning and it seems one of the earliest uses of the word was by Sir Walter Scott in 1816[1]. Scott used the term in reference to Don Quixote, who he considered to be the first biblio-maniac. But today we are here to talk about libraries.

I am thrilled to be here today to celebrate libraries and all they do. I also looked up the English derivation of the word library in the OED. The word seems to have been used by Chaucer in 1374 in old English when he referred to lybrarye: "The walles of thi lybrarye aparayled and wrowht with yuory and with glas".[2]

Libraries are very special places. Let me read you a wonderful passage about the special place libraries have in our lives. I came across this in a book—a REAL BOOK! Made out of paper! The book is a historical novel called "Becoming Mrs. Lewis" by Patti Callahan. It is a story about the intersecting lives of C.S. Lewis and Joy Davidman, and I rate it as a good book. In it, the narrator Joy Davidman describes her experience entering the very old and very large library at the University of Edinburgh in Scotland.

"Libraries are sanctuaries, and the one in Edinburgh was a sacred space with its soaring ceilings and hovering lights, dropping circles of gold on to tables and floors…I stood in the middle, my neck hinged back to stare up. The Corinthian pillars and dark, scarred wooden desks beckoned me to my work. I settled in with books and pad and pen, and began to write. I exhaled with relief: Now this is a place I could work."[3]

At the medical school, we recently celebrated the reopening of the J. Otto Lottes Health Sciences Library—a space that serves not only as a cornerstone of academic support for our students, but also as a hub for collaboration and innovation. This library is not just a space where students can study or access resources—it is where ideas will take shape, where projects will begin, and where new partnerships will form between disciplines.

The new Health Sciences Library is a contemporary library, which looks a lot different from the library at the University of Edinburgh or our grand Ellis Library, which still retains so many features of classic libraries. This is why I, and I am sure many of us, like to escape to Ellis Library and wander through the stacks and lightly run our fingers over rows and rows of books in our favorite sections.

But whether you are in a traditional library full of books or a contemporary one with fewer volumes, the function and purpose is the same. We should be providing an environment that supports academic excellence, critical thinking, collaboration and access to information. And we need to address the evolving needs of our students and faculty.

From advanced study rooms to cutting-edge technology and online resources, libraries need to be designed to enhance learning and foster collaboration. In academic fields where advancements happen rapidly, we know that access to the most current information is essential. Good libraries will continue to be a trusted resource for high-quality information, offering a comprehensive collection of journals, textbooks and databases, many of which are now electronic rather than paper. But whether you access information on paper or electronically, libraries make these and other resources and services available to help you navigate the complex world in your field of study.

I want to tell you about one of the new services of our university library that you may not know about and that the School of Medicine team is excited to be using. This is our digital publishing capability led by Steven Pryor. Our digital publishing unit now has the software from a company called OJS that allows our students and faculty to design and publish our own journals without going through standard, large for-profit publishing houses.
Using this new library technology, in 2024 the School of Medicine launched a new medical journal called Missouri Health. We have now published three issues, and we will be publishing a fourth soon.[4-6] Missouri Health is primarily run by our medical students with faculty supervision. Dr. Dave Arnold, the executive director of the Next-Gen Precision Health initiative is the editor in chief. Fourth-year medical student Jay Devineni along with four other students work closely with Dr. Arnold and other School of Medicine faculty to produce the journals. The initial three issues published all of our students' scientific abstract presentations at various research forums on campus.

This is huge, as our journal is registered in the Library of Congress and each issue has an official Library of Congress DOI number. All of these publications are indexed in Google Scholar. The students can now list these publications on their CVs and applications for residency programs and other jobs. The journal is open-access and there are no charges to publish or obtain the journal online. The authors own the copyrights to whatever they publish—not the publishing house.

As you know, most journals that are open-access charge authors to publish and many use predatory practices to entice authors—many who are junior and green at publishing—to pay to play in their predatory journals.

Missouri Health is crossing a milestone with the next issue, so that we will be publishing full-length articles authored by MU students and their faculty mentors. We are very excited to be moving from abstracts-only to complete manuscripts.

In addition, each cover of Missouri Health depicts a work of art from Mizzou's Museum of Art and Archaeology, and the students work with the museum's deputy director, Marie Nau Hunter in selecting the images for each issue. Therefore, this is a nice example of medicine and science crossing into the humanities realm.

I am very proud of this new journal, and I believe all medical schools should be creating journals

like this so that students, residents and junior faculty can have an avenue to publish their research work. I also think that if every school of medicine did this, it would lessen the control that the large for-profit publishing companies have on all of us.

I should mention that the University of Missouri Digital Publishing Unit can work with any school or college so they can create their own journals. I hope the School of Medicine is just the first at the University of Missouri to leverage this tool.

So thank you to MU Libraries and to Steve Pryor for enabling the School of Medicine to enter the exciting scientific digital publishing space.

Another service I like to remind people of is the amazing University of Missouri Libraries depository, which houses 2 million volumes for the entire University of Missouri System right here in Columbia on Lemone Blvd. This is a cavernous building, and when I toured it with our librarians, I got a chill up my spine standing in this enormous space housing a massive amount of knowledge. Any book or journal can be obtained in less than a day upon request. So while we may have fewer books on site, they are still there. This gives us more room to gather and study and think.

All good libraries are a space where you can sit by yourself and read, study and think. The J. Otto Lottes Health Sciences Library allows us to do just that in the ultra-contemporary chairs and study places. I am particularly fond of the cocoon-like study chairs with the cupola roof and reading light. I often sit in the one next to the atrium and I can see the comings and goings as I read and study and think. But, while the Health Sciences Library has contemporary furniture, it does not have the amazing art that is here in the Ellis Library. What a privilege and treat it is to visit this building and wander through the room with plaster casts of famous sculptures before or after a study session. For the more adventurous students, they can walk down the old iron and marble staircase to the lower level and into the University of Missouri Museum of Art and Archaeology and the Museum of Anthropology.

So now, a visit to the library also allows you to gaze at Minoan artifacts from 1,200 BC or exquisite paintings from the 18th, 19th or 20th centuries. What a great stimulus this is to inspire your brain to kick into gear and come up with new ideas.

I wanted to close with a few of my favorite quotes from one of my academic heroes, Dr. William Osler. Osler was one of the greatest physicians, who changed the practice of medicine in the late 1800s and early 1900s. He was a Canadian who worked first at universities in Montreal, then Philadelphia, then Baltimore and finally in Oxford. In addition to being a brilliant clinician and medical author, he was a library and book aficionado.

Osler said of libraries:
"The organization of a library means effort, it means union, it means progress. It does good to those who start it, who help with money, with time and with the gifts of books. It does good to the young students, with whom our hopes rest. And a library gradually and insensibly molds the profession of a town to a better and higher status."[7]

Another Osler quote I like is focused on medical books:
"To study the phenomena of disease without books is to sail in uncharted seas. While to study books without patients, is not to go to sea at all."[8]

And to end my comments today, this Sir William Osler quote is about what he called "library instructors." Dr. Osler said:
"There should be in connection with ever library a corps of instructors in the art of reading, who would, as a labor of love, teach the young how to read."[9]

I really like that quote because it emphasizes how important all of our library staff are to the success of a library, in our case, at the University of Missouri's academic libraries.

I want to thank our vice chancellor of libraries, Kara Whatley, and all of her directors and staff, who are there daily for our students and faculty as they pursue their careers to make the world a better place and to improve the human condition—which I believe is the mission for universi-

ties. William Osler also said the two great functions of the university are to think and to teach. So we need to support and thank our university libraries, as they are one of the most important ingredients to our success.

Thank you very much for allowing this librobiboliomaniac to speak to you this evening. It is a great honor.

REFERENCES

1. Simpson JA, Weiner ESC. Oxford English Dictionary, 2nd edition. Clarendon Press, Oxford. 2004;2:169.
2. Simpson JA, Weiner ESC. Oxford English Dictionary, 2nd edition. Clarendon Press, Oxford. 2004;8:888.
3. Callahan P. In: Becoming Mrs. Lewis. Thomas Nelson; Nashville, Tennessee, 2018:134-135.
4. Missouri Health. 2024;1(1). https://doi.org/10.32469/mohealth.v1i1
5. Missouri Health. 2024;1(2). https://doi.org/10.32469/mohealth.v1i2
6. Missouri Health. 2025;2(1). https://doi.org/10.32469/mohealth.v2i1
7. Osler W. Counsels and Ideals and Selected Aphorisms. Classics of Medicine Library. Birmingham, Alabama. 1985:158; Also in Aequanimatas in the essay “Some aspects of medical bibliography”, first published 1904.
8. Osler W. Counsels and Ideals and Selected Aphorisms. Classics of Medicine Library, Birmingham, Alabama. 1985:159; Also in Aequanimatas in the essay “Books and men”, first published 1904.
9. Osler W. Counsels and Ideals and Selected Aphorisms. Classics of Medicine Library, Birmingham, Alabama. 1985:159; Also in Aequanimitas in the essay “Books and men”, first published 1904.

Comments to incoming PhD students in the School of Medicine
Translational Biosciences PhD
University of Missouri School of Medicine
August 13, 2025

Comments by Richard J. Barohn, MD
Executive Vice Chancellor for Health Affairs
Hugh E. and Sarah D. Stephenson Dean, MU School of Medicine

As part of your welcoming comments from me into the School of Medicine (SOM) PhD training program1, I want to review with you what I believe are some of the future career pathway options you will have when you graduate with your PhD. I believe as you enter the program it is a good time to begin thinking of these options even though you will not have to make the decision for a number of years.

This graphic shows what I believe are the potential options you will have once you have your PhD. This figure does not include the option of doing more training as a post-doctoral fellow which a number of you may pursue. Post-docs are particularly useful if you plan to have a traditional academic career. The post-doc fellowship range in length from 3 to 5 years.

So let us assume you have your PhD, and you may also have done a post-doc fellowship. The most common path is to take a job in industry. If you pursue this option, there are a number of different roles you can do working for either a large biomedical or pharmaceutical company, or a small one. You can be a research laboratory scientist and continue to work in a research lab as you have done during your PhD training. In training you worked under a PhD faculty mentor. In industry your supervisors will be administrators or other more senior PhD scientists, and you will work on projects important to the company. Another option in industry is to be part of their sales and marketing force. A third option is to become involved in the company's clinical trials unit if the employer has one. Most likely this happens at a pharmaceutical company. Within the clinical trials pathway there are a number of different roles depending on your prior training and your interest, and of course their need. This can include becoming a clinical research associate and working on specific drug or device trials. Other roles are in regulatory management, quality assurance (auditing) and data management. All of these may have entry level positions and with time there usually are promotional opportunities for project manage-

ment.

If you choose to work in academia at a university, again there are a number of options. The traditional scientific role is as a faculty member. This generally comes after a post-doctoral fellowship and having worked in a mentor's laboratory for a number of years. Now you have your own ideas for scientific research, and you want the opportunity to pursue those at a university. Often this involves a tenure -track position as an assistant professor that, if you are successful, can lead in approximately six years to a tenure as an associate professor. Tenure in many ways offers job security for the remainder of your academic career. To obtain tenure and promotion you will need to demonstrate academic success in the form of securing federal grants (usually NIH grants), and scholarly publications, and developed a national reputation in your chosen field. The ultimate goal is to become a full Professor over time.

Not all universities have tenure track as an option for incoming scientist what want to pursue their own research and at these institutions you will be hired as an assistant professor on the non-tenure track. Another option to continue to work in a laboratory and do research at a university is to be a research scientist or research assistant professor. In both of these roles you may again be working in the laboratory or in the research program of an existing senior faculty member at the university, usually one on the tenure track or with tenure. So you may not be pursuing your own scientific ideas. But as I just said, at some universities, the tenure track is not an option immediately out of training, and you can be hired to pursue your own research as a non-tenured track investigator. This is all very dependent on the university. We have seen some PhDs out of training enter the field of clinical research. This can be directly of their PhD depending on what they trained in. But more often it is after working in a traditional wet lab and deciding to move into clinical research after some additional training that may be interesting. In the clinical research category, the scientist can be on the clinical research team enrolling patients in trials, or they can serve on the regulatory team a very important and essential role.

Many PhDs coming out of training and entering their first university job are expected to teach as well. The degree of teaching responsibilities depends on the university, their needs, and the type of department you are in. In schools of medicine, teaching responsibilities may not be emphasized as much as in other schools such as colleges of arts and science where a newly minted faculty member may be expected to have 20 to 50 percent of their time devoted to teaching, often in traditional classroom settings. In schools of medicine, the emphasis is generally on launching your own research career. However this may be changing, and we are now asking our incoming new faculty to expect to do more teaching in their early academic years. Teaching in a school of medicine can involve educating medical students, undergraduate students, or graduate students.
Many PhDs who have worked in research for a number of years can pursue administration career pathways. Administration roles are numerous. One can be as a department chair or vice chair. One can work in the Dean's office as an associate or assistant dean of research. If you begin in a department within the school of medicine that is part of a larger university structure, there are administrative opportunities at even higher levels in the provost's office or the central research office. And if you have spent time in education, there are administrative roles in the various teaching units.
There are career paths other than industry of academia. At any time if one is in either industry or academia, some scientists exit to become entrepreneurs and start up their own company. They can ultimately sell their inventions to a larger company or be absorbed by a larger company, or they can become a large company! There are some bold young scientists who enter the entrepreneur pathway directly out of training. This has become more common in recent years.

I should mention a few other options. There are free standing research institutes where a scientist can be employed. An example in the Kansas City area is Stowers Biomedical Research Institute. Research institutes are engaged in high level science that is similar to the research pursued in academia. Most are non-profit organizations that have been endowed with large sums of money by a donor, and the goal of the institute is to

advance biomedical science, often in a predetermined field.

You can also work as a scientist for the federal government. An example is working in the Department of Veterans Affairs at a VA Medical Center, such as the Truman Veteran Administration medical center in Columbia. Of course there are a number of other governmental agencies where a scientist can work such as the US Military or the National Institutes of Health. Some PhDs obtain further education and go to law school. With a law degree combined with a PhD in science can then lead to a career as a patent lawyer or a leadership position in industry. Short of a law degree, some PhDs can pursue a Master's in Business Administration (MBA) or a Master's of Public Health (MPH).

I listed consulting as another career option, but this will typically come much later after one of the other initial career pathways we have discussed. Welcome to the translational bioscience PhD training program at the University of Missouri School of Medicine. While it may be difficult to visualize where your career may lead after you obtain your PhD, which we all know 4 to 6 years from now. But it is never too early to at least be aware of all of these career options and begin planning.

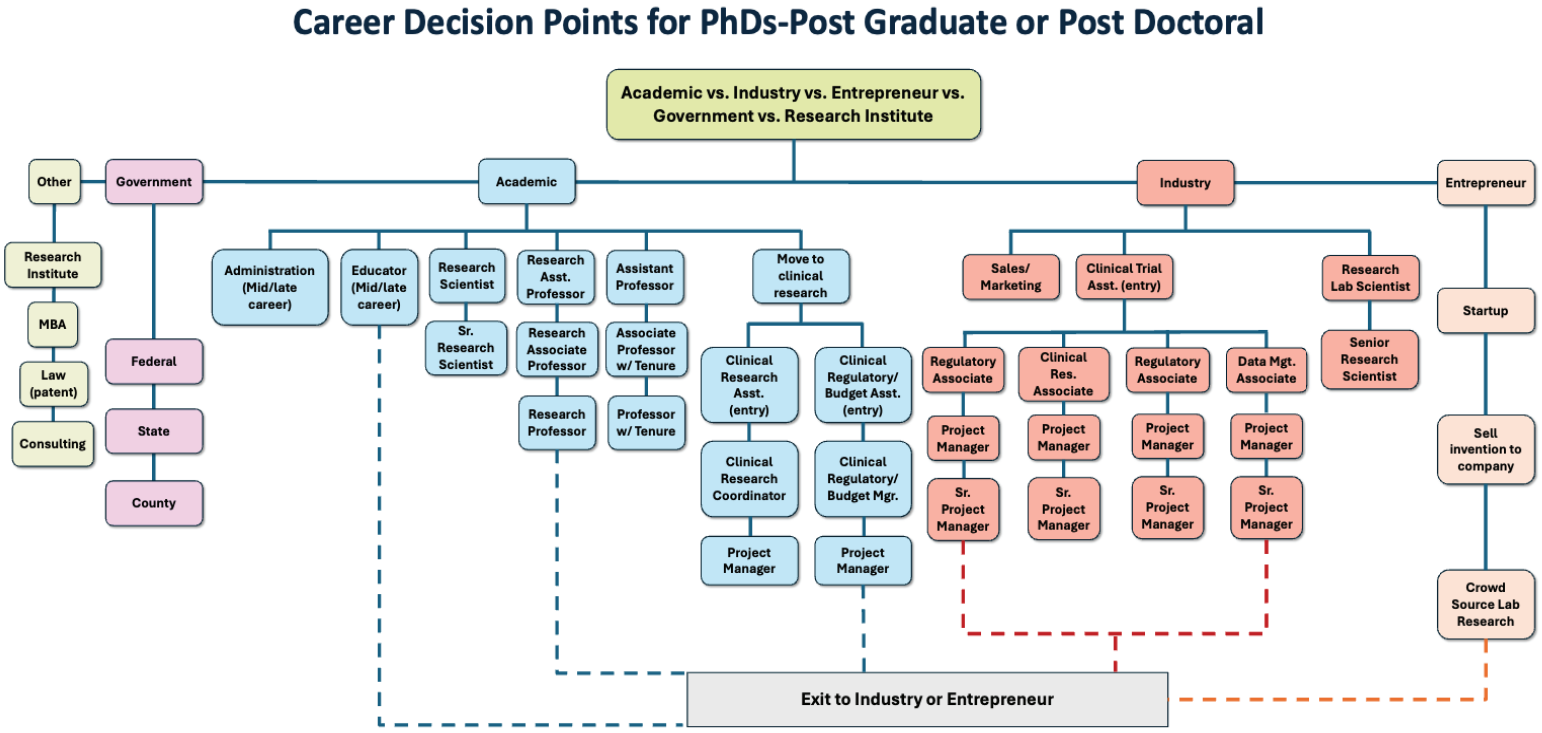

Figure 1. Career Decision Points for PhDs Post-Graduate or Post Doctoral.

REFERENCES

1. Barohn, R. J., Kimminau, K. S., & Brooks, W. M. (2018). Setting Realistic Expectations and Possible Career Pathways for Junior Health Professionals. *Merrill Series on The Research Mission of Public Universities, 10-21.* https://doi.org/10.17161/merrill.2018.9121

Comments to the incoming first-year medical students at the University of Missouri School of Medicine after the annual stethoscope ceremony
University of Missouri School of Medicine
July 30, 2025

Comments by Richard J. Barohn, MD
Executive Vice Chancellor for Health Affairs
Hugh E. and Sarah D. Stephenson Dean, MU School of Medicine

We just had the stethoscope ceremony. In a couple days we will have the white coat ceremony. These are two important annual rites of passage as you begin your medical career. Now I am going to give you all a very short talk about career pathways for physicians. I have never given it to medical students in their first week of medical school. I usually give it to residents or when physicians are finishing their fellowship.

The subtitle of the talk is "What They Never Taught You in Medical School About Career Paths — Until Now". The earlier you hear about career options, the better. You are going to get this talk today, and I will give it again next summer when you start your summer experience. I think it is important to hear it early and often.1

Let's imagine seven years from now if you are going into internal medicine or pediatrics or family medicine which have 3-year residencies. Or ten years from now if you are going into neurosurgery or a surgical subspecialty that has a long residency. You are finishing residency, and maybe you have also done a fellowship, and you are close to 30 years old or older. What career options can you pursue as a physician? That is what this talk is about and that is what this figure shows.

You have chosen your specialty — primary care or not, hospital-based or not — and you are about to launch into your first job. In your final year of training, whether residency or fellowship, you will begin looking at job options. I think of this figure as showing the "universe of job options" for newly minted physicians. The earlier you know about these options, the better.

Today is not decision day. You made your decision when you applied to medical school. You will make another big decision when you apply to residency. You may choose to do a fellowship. Then you will have to make this decision: where will you work?

There are two major pathways of potential job

options for physicians: academic medical centers (like MU Health Care) and non-academic practice.

Non-academic Practice

Traditionally, most doctors end up in non-academic practice. Within this, there are two main options.

The first is traditional private practice. In private practice, you are your own employer. Solo practice is rare now but still possible, both in large and small communities. More commonly, you will join a group practice owned by a group of physicians. You may begin as a partner or you may begin as an employee and become a partner over time. Examples of two large private group practices are the Jefferson City Medical Group in Jefferson City and the Columbia Orthopedic Group (COG) in Columbia.

Private practice can include more than patient care. Some physicians conduct pharmaceutical drug trials, generating income and contributing to research, even though they're not at an academic center. When I set up multicenter trials, I often collaborate with private-practice colleagues who enroll patients.

The second pathway is employment by a non-academic health care system. This is increasingly the most common career option. Regional examples include Boone Health, Mercy in St. Louis and Springfield, CoxHealth healthcare system in Springfield, and HCA Midwest Health in Kansas City. These systems employ many physicians in outpatient, inpatient, and hybrid roles.

Therefore these are the two major options under non-academic practice: private practice and health care system employment.

Academic Medical Centers

The other large category of potential employment for physicians is academic medical centers (AMCs) such as MU Health Care, Barnes-Jewish Christian Healthcare in St. Louis, SSM Health Saint Louis University, or the University of Kansas Health System in Kansas City, Kansas.

Today you can often do the same clinical job at an AMC that you can do at a non-academic health system. Academic medicine used to be mostly tertiary care, with most physicians involved in scholarly activities such as publishing, education, and research. Now, many physicians at AMCs primarily have clinical roles. This is because over the last two generations as AMCs grew and they began taking on more responsibility for primary and secondary clinical care, the role for full-time clinical physicians increased dramatically. The pay gap that once existed between AMCs and non-academic systems has narrowed and in many areas of medicine it has disappeared.

Many physicians feel comfortable at AMCs since that is where they trained as students and residents, and therefore that is often their first job after training.

On the other hand, our medical students frequently spend time training at non-academic medical centers and their mentors and role models are the physicians employed in these settings. Therefore many choose a non-academic health system environment for their careers. For example, our Springfield students train at two outstanding non-academic systems, Mercy and Cox Health.

Administrative and Education Pathways

After a physician is involved in patient care for a number of years, other roles often become available in administration and education. Education roles such as leading medical students, residents, and fellow education more traditionally exist in AMCs. However, many non-academic health systems have also taken on more educational roles for students in residency and leadership positions have been created to lead these programs. Similarly administrative roles for physicians are options that are available at both AMCs and non-academic health systems. Examples include the Chief Medical Officer and the Chief of Staff. Chairs of a department or leaders of service lines are also roles in both settings although some of the duties may vary in an academic vs a non-academic setting.

These administrative and educational pathways often develop gradually and they typically occur in mid or late-career. When serving in these roles, physicians often continue to see patients part-time.

Research Pathways

A minority of physicians pursue careers in research. Most end up at academic centers, though some exceptions exist. For example, one of my cardiology colleagues at Saint Luke's Healthcare System in Kansas City has built a prolific research career outside of a traditional AMC. Interestingly, Saint Luke's Healthcare was just absorbed into the BJC Healthcare system which again shows how the lines between academic and non-academic centers continue to blur.

If you pursue research, you will need to decide how much of your work week will be devoted to research. Some physicians spend 80–90% of their time on research and only 1 or 2 days per week in clinic or surgery. These physicians have a goal of securing NIH and other grants. They are committed to doing a majority of their time in research early in their career and I call this the NIH-focused path.

Physicians in the NIH-focused path can be in "wet labs" (cell culture, animal models, preclinical work) or "dry labs" (natural history outcomes, clinical trials, human data). Success usually requires prior research experience in med school, residency, or fellowship.

Others take a blended path, starting mostly clinical and gradually shifting into research through pharmaceutical trials or grants. This is often called the clinical scholar track. Typically, these physicians initially spend 80% of their time on clinical work and 20% on research. Over time, they can transition into primarily research roles. This is the pathway I took in my career.

The concept of tenure is an old university employment concept. Historically tenure was a tool to protect freedom of speech of faculty. Thus, tenure was developed to ensure that faculty could not be eliminated from their position for expressing unpopular beliefs and without cause. Tenure vs. non-tenure tracks still exist in academia. In the modern era, for physicians, tenure tracks are primarily reserved for physician scientists who pursue an NIH-focused research path. Most physicians in AMCs are on the non-tenure track. The concept of tenured tracks and tenure does not exist in a non-academic medical center. In AMCs, the role of tenure is much less relevant for physicians and generally is not a factor you will be considering when making career decisions unless you pursue an NIH-focused research path.

Other Career Options

Another option is military service, which I personally pursued through the United States Air Force after enrolling in the Health Profession Scholarship Program (HPSP) in medical school. Still other options for employment are in the Veterans' Administration health system and in the Public Health Service (PHS).

Some physicians later pursue master's degrees in business or law degrees, which can lead to administrative or leadership roles such as Chief Financial Officer and Chief Executive Officer in healthcare systems. Other master's programs include Master's of Public Health (MPH) and Master's in clinical and Translational Research (MSCR). These can sometimes be pursued during medical school by taking an extra year or during postgraduate training or during early career positions immediately post training.

Some physicians who initially pursued a research pathway leave academia for industry in large or small pharmaceutical companies and some become entrepreneurs in healthcare and start their own businesses.

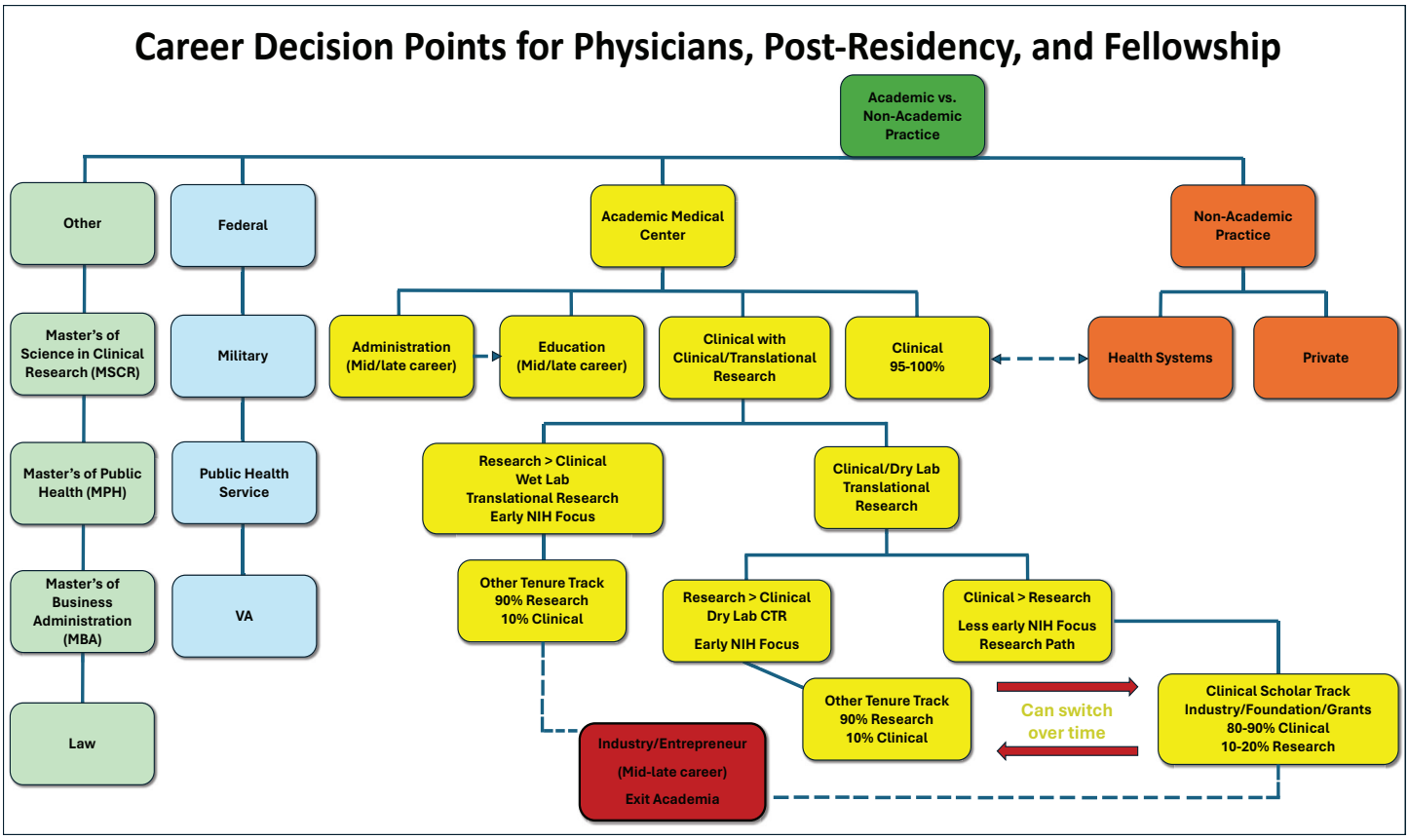

Figure 1. Career Decision Points for Physicians Post-Residency and Fellowship.

REFERENCES

1. Barohn, R. J., Kimminau, K. S., & Brooks, W. M. (2018). Setting Realistic Expectations and Possible Career Pathways for Junior Health Professionals. *Merrill Series on The Research Mission of Public Universities, 10-21.* https://doi.org/10.17161/merrill.2018.9121

University of Missouri School of Medicine commencement speech 2025

Lauren Umstattd, MD

Facial Plastic Surgeon at FACE Leawood

Good morning graduates, families, and faculty.

To the Class of 2025 — you made it. You are now physicians. Doctors. Clinicians. Thinkers. Leaders.

Savor this moment. Breathe it in. You earned it.

I'm a Mizzou Med grad, facial plastic surgeon, and mom of 2 incredible boys - I built my own practice from nothing and I've made a habit of doing things differently. I'm here to talk about what happens when you stop following the rules — and start writing your own

I built a career I love, but I didn't get here by following the rules.

I'm here because I asked better questions.

And that's what I want to talk about: the power of pushing back. The courage to choose differently. The audacity to imagine more. But before we get there — you've got to get through residency. Residency is hard. Brutal, even. You'll be humbled, exhausted. You'll work past the point of depletion. You'll cry in stairwells. You'll doubt yourself on call. You'll stare at a computer monitor wondering if you're cut out for any of this.

Let me reassure you: that doesn't mean you're failing. It means you're becoming.

Residency is a lot. Soak it in. Be curious. Ask all the questions. Arrive early and leave late. Don't just check the boxes or memorize protocols. Chase the questions that keep you up at night. Push deeper. Learn and understand.

In clinic — ask why. In the OR — lock in. Watch how your attendings move. Not just what they do, but how they think.

On call — engage. Learn to trust your judgment. Everything is there to teach you. Every moment. Every mistake. Every win. Every loss. All of it.
Learn from everyone. Your attendings, your coresidents, the RTs, NPs, PAs, pharmacists, and most importantly, the nurses. You will learn more of the nurses than some of your attendings, if you allow them to really teach you.

And while you're learning, you'll also be told to "toughen up," "pay your dues," and "wait your turn." You'll start to think this is what medicine is. But let me tell you something: Residency is not the destination. It's the bridge.

A necessary one — yes. But it is not your final form.
It's the crucible. The grind that sharpens you. So yes — show up. Be diligent. Be present. Be sponge-like. Be hungry. Be teachable. But also: start dreaming. Now.
Not five years from now. Not after fellowship.
Not once you're "established" or "allowed." Today.

Start envisioning the life you want. The career that makes you light up. Not just a job — a calling.

What does that look like for you?

Think about it. Hold it in your mind. Start laying bricks in that direction. Because here's what happens if you don't: the system will dictate your moves and shape you into what it wants. It will hand you a script. Shove a ladder in front of you. Convince you that success looks like assimilation. You don't have to fit in to belong.

I didn't follow the script. I was "supposed" to become a certain kind of doctor. Work for a big hospital. Show up at 6 a.m. for rounds. Operate all day. Defer to the older guy in the room. Dress neutral. Speak when spoken to.
But instead, I wrote my own script and that's why I'm here today - 10 years out from my own graduation.

I left my fellowship early.
I bought a piece of land.
I built my dream.
I created a brand I love.
I hired my own team.
I became the kind of doctor medicine didn't make space for — but desperately needs.

Why?

Because the script you're going to be handed after residency— the one where you grind, comply, and sacrifice your humanity for the sake of being "professional" — that script is broken.

And if you don't wake up, medicine will break you too.

So I'm here to give you a new playbook. Or at the very least, permission to write your own.

Rule #1: Protect Yourself

Not just your body — your mind, your time, your curiosity, your joy. You've spent the last four years learning how to protect patients. But no one taught you how to protect yourself. No one gave you the tools to fend off burnout. To stand firm against bureaucracy. To shield yourself from the emotional erosion of constantly being told you're not enough.

Do not wait until you're bitter to set boundaries.

Protect your joy. Protect your weekends.
Protect your relationships.
Protect your peace like it's a sterile field.

Rule #2: Choose Yourself First

You will be asked — implicitly and explicitly — to put everyone ahead of you. Your patients. Your partners. Your boss. Your imbox. And you'll be praised for doing so. You'll be celebrated for being selfless. You'll be told you're a "team player" as you quietly wither.But here's the truth: If you abandon yourself to serve others, you will eventually have nothing left to give.

You cannot pour from an empty vessel.
Choosing yourself is not selfish. It's sustainable.

Rule #3: Be Loud When They Want You Silent

You will walk into rooms where no one expects you to lead. You will sit in meetings where your ideas are "cute" until someone older — or louder — says the same thing. You will watch mediocrity get promoted because it has a beard and a golf handicap. Speak anyway. Lead anyway.

You don't owe anyone your silence just because they're uncomfortable with your confidence.
Be so good — and so unapologetically yourself — that no one forgets your name.
Especially the ones who pretend not to hear it.

Rule #4: Build the Career You Actually Want

Not the one your program director pushes you towards. Not the one your mom brags about at book club. The one that lights you up. The one that scares you a little.The one that makes you feel like you're creating something that matters.

You want to be a trauma surgeon and a mom of three? Do it.

You want to win Internist of the Year and write sci-fi novels at night? Do it.

You want to write, teach, innovate, disrupt, and lead? Do it.

You are allowed to want more than what they taught you here. Medicine is a foundation — not a cage. And if someone tells you you're "wasting your degree"? Smile. And go waste it in peace.
With freedom, autonomy, and a life you don't need a vacation from.

Rule #5: Learn the Game — Then Play It Your Way

Medicine is a system. A machine. It has rules. It has gatekeepers. It has politics. Learn them. Study the hierarchy. Know who's in the room.

During residency, pay attention. Ask questions. Take notes. Watch where the power lives.
And then — use what you've learned to disrupt the system.Don't just survive it. Don't just "work within it."

Transform it.

We don't need more passive physicians who comply and check the right boxes.
We need provocateurs.
We need architects of something better.
We need you.

Final Rule: Find Your People — and Keep Them Close

Medicine can be lonely.
And you don't get a medal for doing it alone.
When you find your people — the ones who really see you — hang on tight.Text them when a patient dies. Call them when imposter syndrome shows up uninvited. Celebrate each others wins like they're your own. This journey is too long and too hard to walk alone. Find the ones who remind you who you are when you forget. Keep them close.
And never mistake isolation for strength.

The lone-wolf doctor trope is outdated. Dangerous. A lie. We were meant to run — and heal — in packs.

So here you are.
Today feels like a finish line, but it's actually just the beginning.

You've got a degree in hand. And expectations on your shoulders.

And now — you have a choice.

You can follow the script… or you can write your own.
You can stay quiet and safe… or you can rattle the cage.

You can survive in medicine… or you can build a version where you actually thrive.

It won't be easy.
You'll fall.
You'll get back up.
You'll piss someone off just by being exactly who you are.

But if you're bold enough to take the risk?

It will be worth it.

So go.

Defy the script. Shake the system.
Medicine doesn't need more of the same.

It needs you. The real you.

Congratulations, doctors.

Now go make some noise.

CASE REPORT

Venous Stasis Dermatitis as a Risk Factor for Pasteurella Multocida Bacteremia

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ABSTRACT

Pasteurella multocida is a gram-negative bacterium found in the oral flora of dogs and cats. Pasteurella infections are typically localized to skin and soft tissue, but at-risk patients may progress to systemic infections. This report details Pasteurella bacteremia in an elderly patient with chronic venous stasis, highlighting venous stasis dermatitis as a risk factor for systemic infection. Diagnosis was confirmed via blood cultures. Management included ceftriaxone per infectious disease recommendations and was later supported by sensitivities. This case underscores the importance of recognizing chronic skin conditions as risk factors for systemic Pasteurella infections, emphasizing the need for early identification to provide targeted treatment in at-risk patients.

INTRODUCTION

P. multocida is a non-motile, facultative anaerobic, gram-negative coccobacillus that is a normal part of the upper respiratory tract flora of many mammals. It is the most frequent isolate from dog and cat bites and scratches, which are the primary mode of infection and account for approximately 1% of all emergency room visits [1-3].

Most research on *P. multocida* infection focuses on skin and soft tissue infection, which is relatively common and affects otherwise healthy individuals; in contrast, invasive infections (meningitis, endocarditis, peritonitis) are much rarer and affect almost exclusively patients with significant underlying risk factors or disease [4-8]. Prior case reports have not yet identified reliable symptoms, imaging, or laboratory findings to distinguish invasive P. multocida infections from those caused by other pathogens [9,10]. This absence of distinguishing features is concerning is because patients with invasive infections face increased risk of developing *P. multocida* bacteremia, which often onsets in under 24 hours after exposure and has a mortality rate of approximately 30% [7-11].

Previously described predisposing conditions for *P. multocida* bacteremia include liver dysfunction, diabetes mellitus, solid organ transplantation, malignancy, and advanced age [8]. However, these only are present in 67% of diagnosed patients, meaning one-third of patients may not have clear indicators for risk at presentation. Skin exams are a quick and non-invasive means of assessing patients;

however, little research has explored whether dermatologic conditions may be useful in identifying patients at increased risk of *P. multocida* infection.

Between 2 and 6 million Americans have advanced forms of chronic venous insufficiency, notable on physical exam with swelling and hyperpigmented skin changes of the extremities [12]. Chronic venous insufficiency causes vascular and skin barrier damage, ulcer formation, impaired and slowed healing, through the inflammatory changes mediated by leukocyte accumulation, oxidative stress, and matrix-metalloproteinase degradation of the vascular extracellular matrix [13-18]. However, an association between venous stasis, evidenced by skin changes, and *P. multocida* bacteremia has not been previously described.

Case Presentation

A female in her 70s presented to the emergency department (ED) with fever, nausea, and pain in left lower extremity one day after a dog scratch. The patient's medical history included obesity (BMI 68.3), asthma, obstructive sleep apnea, hypertension, hypothyroidism, prior stage 1 breast cancer, and recurrent bacterial and fungal skin infections affecting her lower extremities. At presentation, the patient was not on any immunosuppressive medications. The patient reported that, at baseline, she used a wheelchair for ambulation. She lived at home with her husband, her grandson, her grandson's family and two small dogs. One year prior to this presentation, she was diagnosed with culture-negative cellulitis in the same extremity and so she became concerned when her left leg became red and painful.

In the ED, vital signs showed temperature 37.8 °C, heart rate 124 beats per minute; respiratory rate 20 breaths per minute, blood pressure 139/80, and oxygen saturation of 94%. Physical examination revealed erythema and warmth of a tender left lower extremity extending from the dorsal left foot to the ipsilateral knee along with two <1 cm purpuric puncture wounds on the lateral ankle which drained clear-yellow fluid and blood. Examination of bilateral lower extremities revealed diffuse pink-to-brown darkening of the skin most pronounced inferiorly and anteriorly, with xerotic plaques and overlying white flaking scale (Image 1).

Laboratory studies revealed white blood cells, inflammatory markers, and electrolytes within normal limits; lactate was elevated at 4.2 mmol/L. Chest x-ray demonstrated perihilar/infrahilar-predominant airspace consolidation compatible with pulmonary edema and/or pneumonia. X-ray of tibia and fibula showed posterior fibular cortical indistinction and diffuse regional subcutaneous soft tissue inflammation, suggestive of osteomyelitis (Image 2). Blood cultures were drawn, and the patient was admitted for evaluation of sepsis and cellulitis (Table 1).

The patient was treated empirically with intravenous clindamycin and vancomycin with differential diagnoses including sepsis and osteomyelitis. Two days after admission, blood cultures returned positive for gram-negative rods. MRI showed diffuse subcutaneous edema and overlying soft tissue nodularity of the medial leg without fluid collection or significant osseous hypointensity, and thus imaging was inconsistent with abscess or osteomyelitis. On the third day of admission, blood culture identified the infectious agent as P. multocida.

After identification, clindamycin was discontinued and cefepime was started. A midline IV was placed on day 6 of admission to administer ceftriaxone 2g daily for 14 days, per infectious disease recommendations. Sensitivities returned

after ceftriaxone was initiated but confirmed susceptibility to both penicillin and ceftriaxone.
The patient was discharged on day 15 and was seen two months later in clinic. At that time, her recovery was without complications attributable to the infection.

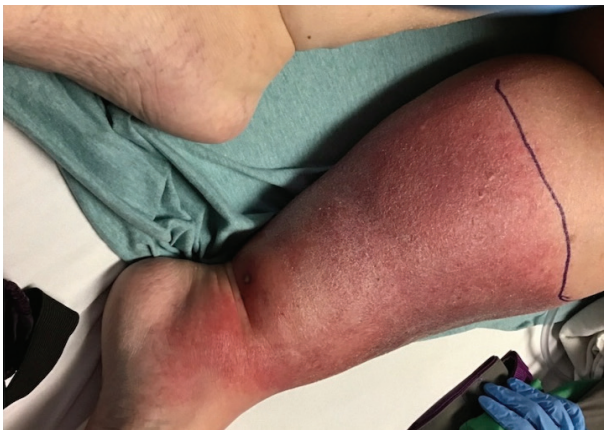

Image 1: Drawn line demarcates hazy borders of skin and soft tissue infection and inflammation on left lower extremity. Purpuric puncture wound draining clear-yellow fluid noted on left lateral ankle. Xerotic plaques and overlying white flaking scale well-visualized, consistent with underlying venous stasis skin changes

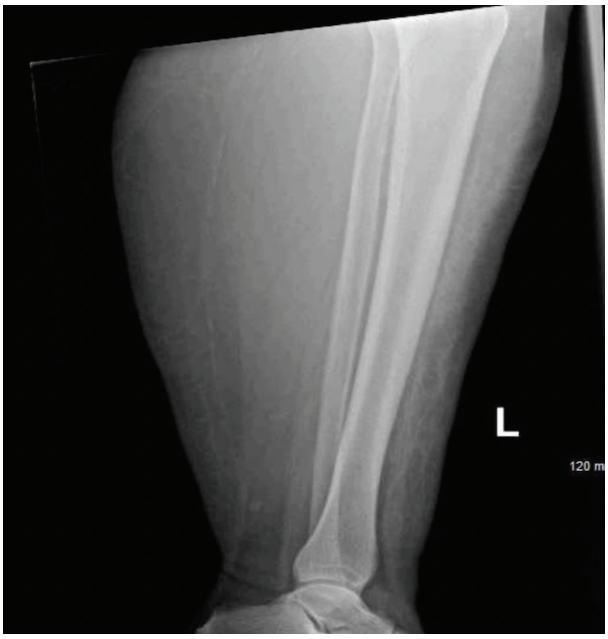

Image 2: Image is negative for subluxation/dislocation, acute fracture. Image positive for subcutaneous edema and moderate osteoarthritis. Demonstrates no radiographic evidence of osteomyelitis.

Discussion

This patient's presentation of tachycardia, hypertension, and suspected cellulitis aligns with existing literature on Pasteurella bacteremia, which is commonly linked to dog or cat exposure and usually arises in the context of skin and soft tissue infection or other invasive disease. Patient's recurrent history of lower extremity cellulitis and recall of recent dog scratch supported infectious etiology, even though patient was alert and oriented, afebrile, and labs showed normal leukocyte count at presentation.

P. multocida, likely transmitted via dog scratch, was determined to be the cause of her illness. While often an infection of skin and soft tissue in immunocompetent persons, invasive infections are almost entirely seen in immunocompromised patients, the elderly or neonatal patients, or those with chronic pulmonary disease. Venous-stasis-induced inflammation and oxidative stress damaged the patient's skin barrier and endothelium, predisposing her to this infection, in addition to previous lower extremity skin and soft tissue infections. Furthermore, the extent of her venous stasis is exacerbated by sedentarism and use of a wheelchair at baseline [19].

Atypical Pasteurella infections, including non-bite transmission, such as in this patient, are associated with increased morbidity and mortality [8]. To avoid rapid progression and severe symptoms, prompt recognition of risk is necessary to avoid severe symptoms, despite risk factors. This highlights the value of thorough patient interviews and the importance of obtaining blood cultures, even in ambiguous cases.

Patient Perspective:

What were the first signs and symptoms you recognized?

"The first thing I noticed was redness and heat right on my left leg. It became painful. It went so fast that that I was kind of fully into the whole infection before I knew what happened. I was sick and running a fever and somewhat out of it – almost delusional. It was a very strong and fast reaction compared to any others I've had. I have problems with MRSA, so any time I get a scratch from my dogs, I watch it pretty close. After I got scratched, I watched it; it was feeling hot. My grandson happened to be visiting and was the one who called my husband. We had to tell him to turn right around and come back. I have a power wheelchair, and our car is the only one that can transport me."

What were your thoughts or concerns while sick?

"I remember being in the hospital pretty well, but I remember when I was first there and talking to the doctors, what I said wasn't what I was actually thinking. It was a little scary and weird. I never had an experience like that before. My brain was really out of it."

"There were a lot of things going on that they were watching me pretty close. The emergency room doctor said I was close to – or I was – septic and that my leg might be need to be removed. I don't have a good recollection of some of this."

What was your experience with treatment?

"Once I started treatment, I started feeling like myself. My leg did hurt, I was in a lot of pain. Some of the pain was brought on by my handling in the hospital because of my hip."

Do you feel that you have fully recovered?

"I feel that I have mostly recovered. There are some things like some of the abilities I had before I went to the hospital [which have not recovered], but it's because of the pain more than what the injury was. My hip has deteriorated over this time."

Have you changed any aspects of your life since hospitalization?

"The biggest thing is maybe a change in attitude. When you go through your worst possible experience, it's something you don't want to go through again. That's part of what

has motivated me to lose weight. I've been working really hard to get healthier, and I've been somewhat successful. I've lost 60 pounds."

Have you changed your relationship with animals since hospitalization?

"Not really. They're family. I just wear my long pants all the time and try to make it heavy enough that they can't scratch through it. I have worked on their behavior a bit so I can avoid repeating the hospitalization."

"The next time I got a scratch, the nurse practitioner I was seeing at the time, instead of waiting to see what would happen, we did mupirocin and fresh dressings every day for a week or two. It didn't get infected. I have some of that on hand, so if I get even a small scratch I just go ahead and use it until I feel it is starting to heal."

Have you changed any aspects of your skin care?

"I haven't made any specific changes to my skin care."

Learning Points:

1. A compromised skin barrier may serve as an independent risk factor for systemic infection.
2. Skin exam is amongst the most rapid means of gaining important information about patients for whom infection is suspected.
3. A detailed history, including animal exposures, should be collected for all patients who present with signs of systemic infections, even if patients do not report a recent bite.
4. In patients with underlying venous stasis skin changes, education on skin hygiene, protection from injury, and inspection of affected limbs may help prevent invasive infections.

Table 1: Patient Results at Presentation. The patient's laboratory findings at presentation are in the table above, alongside corresponding reference limits and units. An asterisk (*) denotes significant results

Vital Signs

Metric	Value	Normal	Units
Temperature*	37.8	36-37.8	Celsius
Heart Rate*	130	60-100	Beats Per Minute
Respiratory Rate*	20	8-20	Breaths Per Minute
SBP NIBP	89	90-139	mmHg
DBP NIBP	64	60-90	mmHg
SpO2	95	88-100	%
BMI	68.3	18.5-24.9	kg/m2

Hematology Profile

Metric	Value	Normal	Units
RBC	4.27	3.9-5.03	x10(12)/L
HGB	14.3	12-15.5	g/dL
HCT	43.8	34.9-44.5	%
MCV	102.6	81.6-98.3	fL
MCH*	33.5	26-33	pg
MCHC*	32.6	32-36	g/dL
RDW SD*	49.7	46.3-46.3	fL
RDW CV	13.2	11.9-15.5	%

PLT	204	150-450	x10(9)/L
WBC	4.13	3-5-10.5	x10(9)/L
Abs Granulocytes	3.76	1.7-7	x10(9)/L
Abs Immature Granulocytes	0.01	0-0.03	x10(9)/L
Abs Lymphocytes*	0.28	0.9-2.9	x10(9)/L
Abs Monocytes*	0.05	0.3-0.9	x10(9)/L
Abs Eosinophils*	0.02	0.05-0.5	x10(9)/L
Abs Basophils	0.01	0-0.3	x10(9)/L

General Chemistry

Metric	Value	Normal	Units
Sodium Level	136	136-145	mmol/L
Potassium Level	3.9	3.5-5.1	mmol/L
Chloride	105	98-107	mmol/L
CO2	21	20-31	mmol/L
Anion gap	14	0-20	mmol/L
Glucose Level	104	70-139	mg/dL
BUN	17	8-23	mg/dL
Creatinine, standardized	0.8	0.5-1	mg/dL
Estimated GFR for Adults*	77	>90	mL/min/1.7
Calcium Level	10	8.3-10.6	mg/dL
Total Protein	7.1	5.7-8.2	g/dL
Albumin Level	3.9	3.4-5	g/dL
Total Bilirubin	1.02	0.3-1.2	mg/dL

Alkaline Phosphatase	58	35-104	U/L
AST-SGOT	31	<=34	U/L
ALT-SGPT	18	10-40	U/L

Immunology/Virology

Metric	Value	Normal	Units
CRP	0.8	<=1.0	mg/dL
Lactic Acid, Plasma*	4.2	0.5-2.2	mmol/L

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REFERENCES

1. Wilson BA, Ho M. Pasteurella multocida: from zoonosis to cellular microbiology. Clin Microbiol Rev. 2013 Jul;26(3):631-55. PMID: 23824375; PMCID: PMC3719492.
2. 2. Owen CR, Buker EO, Bell JF, Jellison WL. Pasteurella multocida in animals' mouths. Rocky Mt Med J. 1968 Nov;65(11):45-6. PMID: 5749275.
3. 3. Oehler RL, Velez AP, Mizrachi M, Lamarche J, Gompf S. Bite-related and septic syndromes caused by cats and dogs. Lancet Infect Dis. 2009 Jul;9(7):439-47. Erratum in: Lancet Infect Dis. 2009 Sep;9(9):536. PMID: 19555903.
4. 4. Vesza Z, Boattini M, Pinto M, Marques da Silva P. Pasteurella infections in a tertiary centre - from cellulitis to multiple-organ failure: Retrospective case series. SAGE Open Med Case Rep. 2017 Dec 19;5:2050313X17748286. PMID: 29318015; PMCID: PMC5753917.
5. 5. Arons MS, Fernando L, Polayes IM. Pasteurella multocida--the major cause of hand infections following domestic animal bites. J Hand Surg Am. 1982 Jan;7(1):47-52. PMID: 7061808.
6. 6. Martin TCS, Abdelmalek J, Yee B, Lavergne S, Ritter M. Pasteurella multocida line infection: a case report and review of literature. BMC Infect Dis. 2018 Aug 23;18(1):420. PMID: 30139329; PMCID: PMC6108108.
7. 7. Weber DJ, Wolfson JS, Swartz MN, Hooper DC. Pasteurella multocida infections. Report of 34 cases and review of the literature. Medicine (Baltimore). 1984 May;63(3):133-54. PMID: 6371440.
8. 8. Chatelier E, Mahieu R, Hamel JF, Chenouard R, Lozac'h P, Sallé A, Kouatchet A, Martin L, Lavigne C, Pailhoriès H, Urbanski G. Pasteurella bacteraemia: Impact of comorbidities on outcome, based on a case series and literature review. Int J Infect Dis. 2020 Mar;92:89-96. Epub 2020 Jan 8. PMID: 31926353.
9. 9. Williams KH, Jagadish A, Shah R. A Case of Pasteurella Bacteremia in a Patient With Hepatocellular Carcinoma. Cureus. 2023 Dec 8;15(12):e50161. doi: 10.7759/cureus.50161. PMID: 38186515; PMCID: PMC10771712.
10. 10. Boadu C, Hernandez A, Zeidan B Jr, Young JT, Frunzi J. Pasteurella multocida Bacteremia in an Immunocompromised Patient After Multiple Cat Scratches. Cureus. 2021 Jan 27;13(1):e12938. doi: 10.7759/cureus.12938. PMID: 33654617; PMCID: PMC7916639.
11. 11. Giordano A, Dincman T, Clyburn BE, Steed LL, Rockey DC. Clinical Features and Outcomes of Pasteurella multocida Infection. Medicine (Baltimore). 2015 Sep;94(36):e1285. PMID: 26356688; PMCID: PMC4616664.
12. 12. White JV, Ryjewski C. Chronic venous insufficiency. Perspect Vasc Surg Endovasc Ther.

2005 Dec;17(4):319-27. PMID: 16389426.

13. 13. Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, Lohr JM, McLafferty RB, Meissner MH, Murad MH, Padberg FT, Pappas PJ, Passman MA, Raffetto JD, Vasquez MA, Wakefield TW; Society for Vascular Surgery; American Venous Forum. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2011 May;53(5 Suppl):2S-48S. PMID: 21536172.
14. 14. Brunner F, Berzigotti A, Bosch J. Prevention and treatment of variceal haemorrhage in 2017. Liver Int. 2017 Jan;37 Suppl 1:104-115. PMID: 28052623.
15. 15. Thomas PR, Nash GB, Dormandy JA. White cell accumulation in dependent legs of patients with venous hypertension: a possible mechanism for trophic changes in the skin. Br Med J (Clin Res Ed). 1988 Jun 18;296(6638):1693-5. PMID: 3135881; PMCID: PMC2546087.
16. 16. Sundaresan S, Migden MR, Silapunt S. Stasis Dermatitis: Pathophysiology, Evaluation, and Management. Am J Clin Dermatol. 2017 Jun;18(3):383-390. PMID: 28063094.
17. 17. Wenk J, Foitzik A, Achterberg V, Sabiwalsky A, Dissemond J, Meewes C, Reitz A, Brenneisen P, Wlaschek M, Meyer-Ingold W, Scharffetter-Kochanek K. Selective pick-up of increased iron by deferoxamine-coupled cellulose abrogates the iron-driven induction of matrix-degrading metalloproteinase 1 and lipid peroxidation in human dermal fibroblasts in vitro: a new dressing concept. J Invest Dermatol. 2001 Jun;116(6):833-9. PMID: 11407968.
18. 18. Bergan JJ, Schmid-Schönbein GW, Smith PD, Nicolaides AN, Boisseau MR, Eklof B. Chronic venous disease. N Engl J Med. 2006 Aug 3;355(5):488-98. PMID: 16885552.
19. 19. Suehiro K, Morikage N, Murakami M, Yamashita O, Ueda K, Samura M, Hamano K. A study of leg edema in immobile patients. Circ J. 2014;78(7):1733-9. Epub 2014 Apr 30. PMID: 24790031.
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CASE REPORT

Safety And Efficacy Of Cenobamate In Pregnancy: A Case Report

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ABSTRACT

Seizures remain the most frequent major neurologic complication during pregnancy, affecting 0.3% to 0.8% of all gestations. In clinical practice, the risk of seizures during pregnancy is weighed against the risks of antiseizure drug (ASD) exposure (e.g. teratogenicity, congenital malformations, developmental, and intrauterine growth). With the advent of novel ASDs, further research into the specific risks of these novel medications during pregnancy is warranted. Cenobamate, an ASD approved by the Food and Drug Administration (FDA) for focal onset epilepsy in adults, is highly efficacious, however, all trials of this ASD to date excluded pregnant and lactating subjects. Thus, we present the case of a young female patient with medically refractory epilepsy who elected to continue cenobamate throughout two of her pregnancies and lactation. Our patient had a significant reduction in the frequency of her seizures. There were no complications during either pregnancy, delivery or postpartum. While a single case experience does not establish the safety and efficacy of cenobamate during pregnancy/lactation, patients of childbearing age who are currently considering or already taking cenobamate may benefit from knowledge regarding our patient's experience.

INTRODUCTION

Half a million women suffering from epilepsy are of childbearing age[1]. One-third of pregnant women with epilepsy will have an increase in seizure frequency during their pregnancy. Epilepsy in the pregnant population confers an elevated risk of adverse obstetric outcomes[2]. These women are at higher risk of obstetric hemorrhage, spontaneous miscarriage, and hypertensive disorders. From a pediatric standpoint, five out of every thousand births will be to a mother suffering from epilepsy[1]. In the United States, roughly 25,000 children per year are born to mothers suffering from epilepsy[3]. Complications in the offspring include increased risk of stillbirth, preterm birth, small for gestational age at birth, low Apgar score at 5 minutes, neonatal hypoglycemia, neonatal infection, respiratory distress syndrome, and major congenital malformations (3x higher risk than the general population). The long-

term neurobehavioral development of the child may also be significantly affected[3,4]. Despite these risks, sufficient data regarding the management of epilepsy in pregnancy is lacking[1].

Cenobamate (YKP3089) is an antiseizure drug (ASD) that has demonstrated higher seizure-free rates than any other anti-epileptic in the last 30 years[5]. The safety and efficacy of cenobamate in the obstetric population are unknown[6]. We present the first documented use of cenobamate in a pregnant and lactating patient suffering from medically refractory, intractable focal onset epilepsy with impaired awareness.

Case Presentation

A patient in her early 30s, suffering from medically refractory, intractable focal onset epilepsy with impaired awareness was referred to our epilepsy clinic. At the time, she was suffering breakthrough seizures characterized by right arm stiffening, aphasia, and unresponsiveness lasting for about 60 seconds at a time. Her spells were followed by postictal confusion and occurred once a week despite being compliant with Levetiracetam 1500mg bid and Lacosamide 200mg bid. Previously, treatments including Topiramate, Lamotrigine, Carbamazepine, Oxcarbazepine, and scheduled Clonazepam were attempted, all of which failed to reduce the frequency of her seizures.

Investigations: Prior to the onset of her first pregnancy, workup with continuous EEG monitoring was remarkable for left temporal sharps and occasional lateralized periodic discharges (LPDs) localized to the left cerebral hemisphere. An MRI Brain had also been obtained (Figure 1).

Treatment: Our patient was started on cenobamate and had reached 100mg daily dose (7th week of titration) when she was confirmed to be 7 weeks and 5 days pregnant in her first pregnancy. The risks and benefits of continuing cenobamate were discussed and the patient was informed of the lack of data regarding safety/efficacy in the setting of pregnancy/lactation. The patient expressed an adequate understanding of the same and requested to be continued on the medication throughout her pregnancy. Cenobamate was gradually titrated to 200mg daily by 12 weeks of gestation and her folic acid was increased to 4mg. Maternal and fetal monitoring was done via frequent outpatient visits.

Maternal Outcomes: During the first pregnancy, the patient's seizure frequency reduced to less than one per week and the duration of her postictal confusion was notably shorter, a notable improvement from her weekly seizures prior to initiating cenobamate. After the first delivery, her seizure frequency reduced further to one spell every other month. The patient's seizures remained well controlled approximately one year after delivery, and the patient became pregnant again. She continued cenobamate 200mg during this second pregnancy and both lactation periods. Her seizure frequency remained under one spell every other month during this second pregnancy and after delivery. Two months after the second delivery, the patient denies experiencing any complications. The patient now reports she has been seizure free for 11 months. Of note, the patient breastfed (for three and two months, respectively) and supplemented with formula for both children.

Pediatric Outcomes: For the first child, antenatally fetal heart tones were charted as within normal limits from 11 weeks to birth (143-170bpm). The patient underwent 11 antenatal ultrasounds with normal non-stress tests and biophysical profiles (10/10 or 8/8 charted), appropriate fetal growth tracking with gestational age (estimated fetal weight

percentile ranging from 36th – 62nd), and appropriate amniotic fluid index (within normal limits at each ultrasound). Anatomy scan and cardiac echocardiogram were both normal. For the second child, antenatally fetal heart tones were charted as within normal limits from 11 weeks to birth (133-175 bpm). The patient underwent 11 antenatal ultrasounds with normal non-stress tests and biophysical profiles (10/10 or 8/8 charted), appropriate fetal growth tracking with gestational age (estimated fetal weight percentile ranging from 16th – 39th), and appropriate amniotic fluid index (within normal limits at each ultrasound). Anatomy scan and cardiac echocardiogram were both normal, excluding a circumvallate placenta. Since birth, both children been closely followed by a pediatrician. Their birth weights were 3.6kg and 3.7kg respectively, both determined to be within normal limits by the admitting pediatricians. At the first child's most recent well child check, they were in the 85th percentile for weight and 93rd percentile for height and met all 24-month developmental milestones. On physical exam, no neurological or cardiopulmonary abnormalities were appreciated. The second child, at the most recent well child check, was tracking at the 99th percentile for weight and length, and met all sixth month developmental milestones including: able to sit without support, able to bear weight on legs when pulled up to stand, able to roll over, able to reach for toys and pull to midline, had enjoyment, and laughs, smiles, and squeals. On physical exam, no neurological or cardiopulmonary abnormalities were appreciated.

Discussion

Current guidelines acknowledge that the management of epilepsy in pregnancy is based on observational studies.[1] Older, yet highly effective, medications such as phenobarbital and valproic acid are associated with an increased adverse risk-to-benefit ratio.[7] Lamotrigine, levetiracetam, lacosamide, and oxcarbazepine have been the preferred agents in the pregnant population due to lower rates of teratogenicity.[3] However, for medically refractory patients, there is little data regarding newer, more efficacious agents such as cenobamate.

Cenobamate is a highly efficacious anti-epileptic that was approved by the Food and Drug Administration (FDA) in 2019 for use as adjunctive therapy in adults with focal onset epilepsy.[8] Cenobamate's efficacy was proven in 2 large randomized, multicentric, double-blind clinical trials (NCT01866111 and NCT01397968). Both trials demonstrated a dose-dependent reduction in seizure frequency by up to 55% (p-value < 0.001) when cenobamate was used as adjunctive therapy in patients suffering from medically refractory focal onset seizures. A high responder rate of >40% and a reduction of seizure frequency early in the titration of the medication attests to its potential.[9,10] The medication has since demonstrated higher seizure-free rates than any other anti-epileptic in the last 30 years.[5] Said efficacy may be secondary to cenobamate's multiple different mechanisms of action (Figure 2).[11-13]

Pregnant and lactating humans have been excluded from all trials involving cenobamate to date.[6] Animal studies demonstrated that the highest tested dose of cenobamate (60 mg/kg/day in rats and 36 mg/kg/day in rabbits) resulted in increased embryo-fetal mortality, reduced birth weight, incomplete ossification, and visceral malformations. Such high doses were also directly toxic to the mothers.[14] Dose-independent adverse effects on the offspring included neurocognitive and reproductive dysfunction. Per the FDA-approved cenobamate label "maternal plasma exposure at the no-effect dose for adverse effects on embryo-fetal development was less than that

in humans at the maximal recommended human dose of 400 mg."[14] A large limitation of the animal studies is that the complete teratogenic potential could not be assessed due to the high rate of embryo-fetal deaths. Currently, the FDA recommends that the patient be counseled to inform the prescribing physician if they are pregnant or intend to become pregnant.[14] An expert panel led by Steinhoff et al further advised that if a patient becomes pregnant while on cenobamate, the decision to change to another anti-epileptic may be considered.[15]

There is no data regarding the use of cenobamate during lactation. The Drugs and Lactation Database, advises that the use of cenobamate is not a reason to discontinue breastfeeding, although a change to a different anti-epileptic may be considered.[16]

Our patient had a reduction in her seizure frequency after cenobamate was added to her anti-epileptic regimen. She elected to continue the medication during her pregnancies and lactation. Despite this, she had two unremarkable pregnancies, deliveries, and postpartum periods. Additionally, both children have met developmental milestones and continued to grow appropriately. This data was shared with the North American Anti-Epileptic Drug (AED) Pregnancy Registry. While a single case experience does not establish the safety and efficacy of cenobamate during pregnancy/lactation, patients of childbearing age who are currently considering or already taking cenobamate may benefit from knowledge regarding our patient's experience.

Moving forward, a larger study population involving pregnant and nursing humans is needed to definitively establish the risk-to-benefit ratio of cenobamate in the obstetric population. Furthermore, it is important to recognize that the levels of ASDs during pregnancy are highly dynamic. Future studies should aim to define better how the plasma levels of cenobamate fluctuate across trimesters. Lastly, Patients who use ASDs during pregnancy should be encouraged to submit their experiences to large databases such as the North American AED Pregnancy Registry such that it may be used to establish trends and develop a robust cohort.

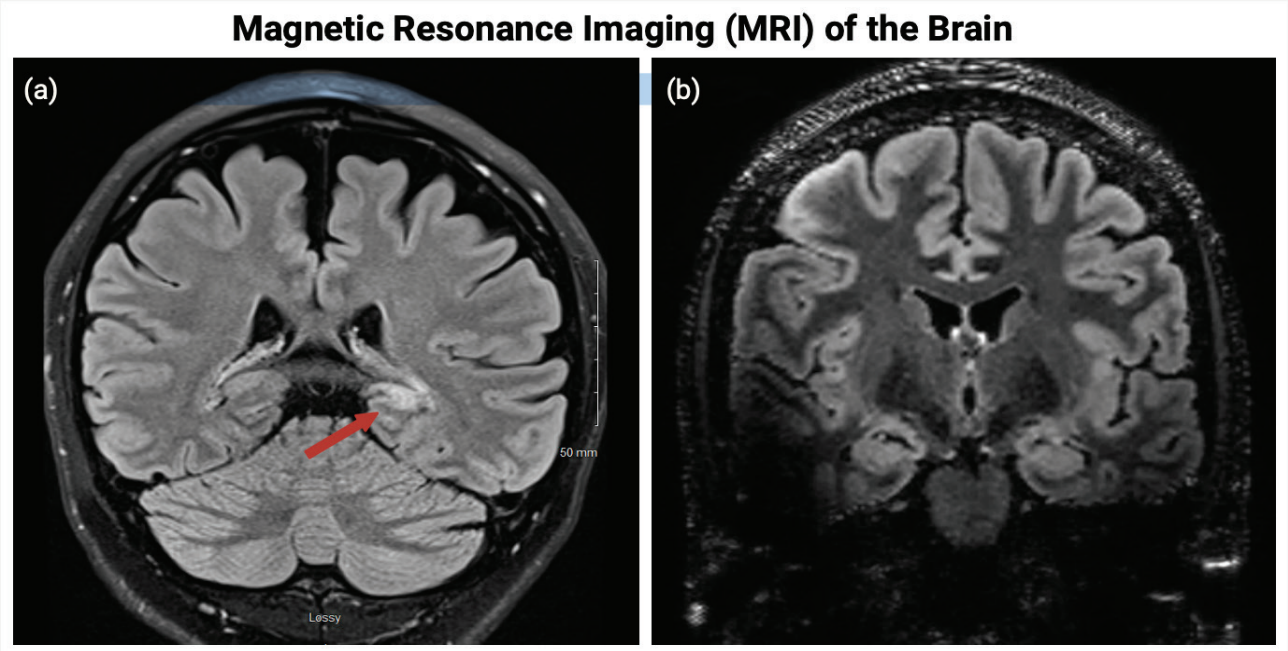

Figure 1: The above images show coronal sections of MRI brain in (a) our patient and allows for comparison to (b) a healthy, age-matched control. The red arrow point to an area of subtle T2-Fluid Attenuation Inversion Recovery (FLAIR) hyperintensity within the left mesial temporal lobe of (a) our patient. These findings are consistent with left mesial temporal lobe sclerosis, a common finding seen in patients with focal epilepsy.

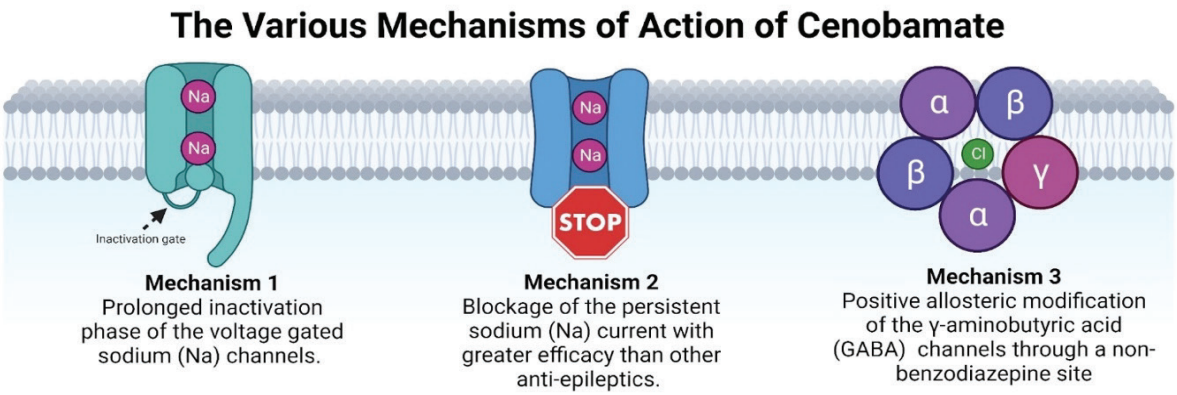

Figure 2: Cenobamate's ability to act on sodium channels and GABA receptors make it a unique anti-seizure agent.11-13

Conflict of Interest: KA was a member of the SK Life Science, inc. (SKLSI) speakers' bureau from 2020-2022, which overlapped with this patient's care.
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REFERENCES

1. Harden CL, Meador KJ, Pennell PB, et al. Management issues for women with epilepsy-Focus on pregnancy (an evidence-based review): II. Teratogenesis and perinatal outcomes: Report of the Quality Standards Subcommittee and Therapeutics and Technology Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Epilepsia. 2009;50(5):1237-1246. doi:10.1111/j.1528-1167.2009.02129
2. O'Connor SE, Zupanc ML. Women and epilepsy. J Pediatr Pharmacol Ther. 2009;14(4):212-220. doi:10.5863/1551-6776-14.4.212.
3. Li Y, Meador KJ. Epilepsy and Pregnancy. Continuum (Minneap Minn). 2022;28(1):34-54. doi:10.1212/CON.000000000000105.
4. Viale L, Allotey J, Cheong-See F, et al. Epilepsy in pregnancy and reproductive outcomes: a systematic review and meta-analysis. Lancet. 2015;386(10006):1845-1852. doi:10.1016/S0140-6736(15)00045-8.
5. Abou-Khalil BW. Update on Antiseizure Medications 2022 [published correction appears in Continuum (Minneap Minn). 2023 Jun 1;29(3):995]. Continuum (Minneap Minn). 2022;28(2):500-535. doi:10.1212/CON.000000000000110.
6. Buckley CT, Waters OR, DeMaagd G. Cenobamate: A New Adjunctive Agent for Drug-Resistant Focal Onset Epilepsy. Ann Pharmacother. 2021;55(3):318-329. doi:10.1177/1060028020941113.
7. Yerby MS. Pregnancy and epilepsy. Epilepsia. 1991;32 Suppl 6:S51-S59. doi:10.1111/j.1528-1157.1991.tb05893.
8. Specchio N, Pietrafusa N, Vigevano F. Is Cenobamate the Breakthrough We Have Been Wishing for?. Int J Mol Sci. 2021;22(17):9339. Published 2021 Aug 28. doi:10.3390/ijms22179339.
9. Krauss GL, Klein P, Brandt C, et al. Safety and efficacy of adjunctive cenobamate (YKP3089) in patients with uncontrolled focal seizures: a multicentre, double-blind, randomised, placebo-controlled, dose-response trial [published correction appears in Lancet Neurol. 2020 Mar;19(3):e3]. Lancet Neurol. 2020;19(1):38-48. doi:10.1016/S1474-4422(19)30399-0.
10. Chung SS, French JA, Kowalski J, et al. Randomized phase 2 study of adjunctive cenobamate in patients with uncontrolled focal seizures. *Neurology*. 2020;94(22):e2311-e2322. doi:10.1212/WNL.0000000000009530.
11. Nakamura M, Cho JH, Shin H, Jang IS. Effects of cenobamate (YKP3089), a newly developed anti-epileptic drug, on voltage-gated sodium channels in rat hippocampal CA3 neurons. *Eur J Pharmacol*. 2019;855:175-182. doi:10.1016/j.ejphar.2019.05.007.
12. Guignet M, Campbell A, White HS. Cenobamate (XCOPRI): Can

preclinical and clinical evidence provide insight into its mechanism of action?. Epilepsia. 2020;61(11):2329-2339. doi:10.1111/epi.16718.
13. Sharma R, Nakamura M, Neupane C, et al. Positive allosteric modulation of GABAA receptors by a novel antiepileptic drug cenobamate. Eur J Pharmacol. 2020;879:173117. doi:10.1016/j.ejphar.2020.173117.
14. Xcopri [package insert]. Paramus (NJ): SK Life Science, Inc; 2019.
15. Steinhoff BJ, Rosenfeld WE, Serratosa JM, et al. Practical guidance for the management of adults receiving adjunctive cenobamate for the treatment of focal epilepsy-expert opinion. Epilepsy Behav. 2021;123:108270. doi:10.1016/j.yebeh.2021.108270.
16. Cenobamate. In: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; August 18, 2021.

ORIGINAL RESEARCH

Physical Therapy on Postoperative Day Zero Following Spine Surgery is Associated with Decreased Length of Stay

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ABSTRACT

Objective: Postoperative LOS is a major factor in overall cost for spine surgery, and its duration often depends on discharge clearance from PT. We sought to compare postoperative length of stay (LOS) for patients who initiated physical therapy (PT) on postoperative day (POD) 0 versus POD 1 following cervical or lumbar spine surgery.

Methods: A retrospective review was conducted of 710 patients who underwent elective, inpatient cervical or lumbar spine surgery at 1 institution from 2011-2019. Patients were categorized by postoperative PT timing, with POD 0 defined within 24 hours postoperative. Patients were excluded if admitted under trauma visit, admitted to ICU before discharge for observation or complications, or had qualifying surgery >2 levels (lumbar) or <2 levels (cervical). Results were analyzed using R (R Foundation for Statistical Computing, Vienna, Austria).

Results: In both surgery groups, there was no significant difference between POD 0 and POD 1 cohorts regarding: age, sex, BMI, preoperative ambulation device, discharge destination, or operative approach and fusion levels (for cervical patients). In both groups, median LOS difference was large enough to be of statistical significance. Among lumbar surgery patients, the LOS was 8.9 hours greater for POD 1 PT compared to POD 0 PT (median 65.3 hours for POD 0 PT [interquartile (IQ) range, 43.7-74.6] vs 74.2 hours for POD 1 PT [IQ range 51.6-99.8]; ($P < 0.001$). Among cervical patients, the LOS was 25.7 hours greater for POD 1 PT compared to POD 0 PT (median 46.8 hours for POD 0 PT [IQ range, 25.7-75.4] vs 72.5 hours for POD 1 PT [IQ range 46.8-101.3], ($P < 0.0001$). The difference in distribution of postoperative nights spent in the hospital was also statistically significant for lumbar surgery patients ($P = 0.002$) and cervical patients ($P < 0.001$). None of the POD 1 PT lumbar patients were discharged on POD 1, compared to 18.3% of lumbar patients who initiated PT on POD 0. Among cervical patients, 8.3% of patients who initiated PT on POD 1 were discharged on POD 1, compared to 21.3% of cervical patients who initiated PT on POD 0.

Conclusion: Our study demonstrated a statistically significantly lower postoperative LOS when PT was initiated on POD 0 versus POD 1, suggesting an association between earlier PT and earlier discharge.

INTRODUCTION

Cervical and lumbar spine surgery are common procedures in orthopaedic surgery.[1-4] As such, these procedures continue to increase annually.[5, 6] Lowering the cost of these procedures remains an important goal as patients and payors demand lower healthcare costs and improved quality.[7] This has led to a rapid interest in enhanced recovery protocols (ERPs), which focus on expedited recovery and patient discharge through a combination of patient education, multimodal analgesia, limiting unnecessary drains and dressing changes, and early physical therapy (PT). However, the significance of early PT in optimizing early discharge is not well elucidated.

The postoperative inpatient length of stay (LOS) is a major factor in the overall cost of elective spine procedures, and recent studies have attempted to enact peri-operative protocols in order to reduce costs and improve the value of care.[8, 9] While the duration of post-operative hospitalization may be affected by PT protocols and discharge often depends on clearance from the therapy team, there is a paucity of literature on the impact of physical therapy on LOS. Discharge clearance is determined by the therapist's evaluation of the patient's ability to ambulate safely at a level that meets their post-discharge needs (e.g., stairs to enter the home, transferring from a walker to bed or chair). If a patient is unable to mobilize safely, their postoperative inpatient stay continues until the therapist can determine that the patient is safe for discharge, or they qualify for placement into an inpatient rehabilitation facility. As such, the physical therapist is often the team member who makes the final determination when a patient is medically safe for discharge postoperatively. One potential strategy to reduce inpatient LOS and its associated costs is early initiation of inpatient PT, starting immediately on postoperative day 0 (POD 0).[10-12] While the literature on immediate initiation of postoperative PT for spine patients is scarce, previous authors have demonstrated that PT intervention on POD 0 shortened hospital LOS for both total hip and total knee arthroplasty patients.[12]

The objective of this study is to determine whether inpatient cervical fusion and lumbar laminectomy and fusion patients who started formal PT on POD 0, instead of POD 1, had a shorter postoperative LOS as measured continuously in hours and overall number of nights spent in the hospital.

METHODS

Following approval by the institutional review board, a retrospective review of prospectively collected data identified 710 patients who underwent elective, inpatient ≥2 level anterior cervical discectomy and instrumented fusion (ACDF), ≥2 level posterior cervical instrumented fusion +/- laminectomy, or 1-2 level lumbar laminectomy ± posterior lumbar fusion ± instrumentation at a single center between 2011 to 2019. The study includes 13 spine surgeons at our institution. Exclusion criteria consisted of: (1) incomplete data in the electronic medical record, (2) admission under a trauma visit, (3) admission to the intensive care unit (ICU) between surgery and discharge for observation or complications, (4) lack of formal PT encounter before discharge, and (5) had surgery involving >2 levels (lumbar patients) or <2 levels (cervical patients). Demographics, intraoperative, and postoperative variables were collected. Demographic information included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, Charlson Comorbidity Index (CCI), insurance type (i.e., Medicare, private insurance), comorbidities (e.g., diabetes), use of a preoperative ambulation aid (i.e., cane, walker, or wheelchair), and postoperative discharge destination (i.e., home, inpatient rehabilitation). All patients underwent surgery under general anesthesia in the prone (lumbar or posterior cervical surgery) or supine (ACDF) position on a Jackson table. Intraoperative variables included the number of levels fused and anterior, posterior, or combined approach. Foley catheters placed intraoperatively were removed prior to transfer to the postoperative recovery unit. Patients received our institution's postoperative pain regimen, which included anti-inflammatories, acetaminophen, muscle relaxers, and opioid analgesics, including as needed IV medications available for breakthrough pain. Postoperative Patient Controlled Analgesia (PCA) was not routinely used. Patients were categorized by timing of postoperative PT, with POD 0 defined as within 24 hours after surgery as documented in the medical record under surgery stop times and initial PT encounter times. Postoperative care did not differ between groups except regarding their timing of PT initiation.

Statistical Methods

Data were checked for quality and completeness. Summary statistics for continuous variables were mean and standard deviation or median and interquartile range. Categorical variables were summarized using

frequencies and percentages. Bivariate analysis used Chi-square tests of independence or Fisher's Exact tests, if Chi-square assumptions were not met. For continuous variables, normality was tested using a Shapiro-Wilk test and a two-sample t-test or Mann-Whitney test was used to determine differences across POD groups. Data were analyzed using R version 4.0.2 with two-sided alpha < 0.05 considered significant.

RESULTS

A total of 710 patients (374 cervical and 336 lumbar) met inclusion criteria. Among lumbar patients, formal PT was initiated on POD 0 for 202 patients, and POD 1 for 134 patients (Table 1). For those who received lumbar surgery, there were no significant differences between POD 0 and POD 1 groups regarding age (57.9 ± 14.4 years vs. 58.4 ± 14.3 years, P = 0.66), sex (45.5% male vs. 52.2%, P = 0.28), BMI (33.2 ± 7.8 kg/m^2 vs. 31.7 ± 5.8, P = 0.23), Charlson Comorbidity Index (CCI) classification (CCI 1.03±1.12 vs. 1.27 ± 1.55, P=0.56), ASA classification (ASA 1 or 2 for 43.1% vs. 39.6%, P = 0.58), preoperative use of ambulation aid (18.3% vs. 12.7%, P = 0.22), or discharge destination (discharge home 88.6% vs. 85.1%, P = 0.61) (Table 1). Among cervical patients, formal PT was initiated on POD 0 for 240 patients, and POD 1 for 134 patients (Table 1). Similarly, among cervical patients, there were no significant differences between POD 0 and POD 1 groups regarding age (57.7 ± 11.0 years vs. 57.8 ± 14.3 years, P = 0.98), sex (55.8% male vs. 47.8%, P = 0.16), BMI (31.2 ± 7.3 kg/m^2 vs. 30.4 ± 7.2, P = 0.31), Charlson Comorbidity Index (CCI) (CCI 1.34 ± 1.57 vs. 1.43 ± 1.76, P=0.78), ASA classification (ASA 1 or 2 for 35.0% vs. 34.3%, P = 0.99), preoperative use of ambulation aid (29.2% vs. 36.8%, P = 0.17), preoperative myelopathy (59.4% vs 63.4%, P = 0.51), or discharge destination (discharge home 81.3% vs. 71.6%, p=0.08) (Table 1). However, there was a significant difference between the POD 0 PT and POD 1 PT among cervical patients with private insurance (30.4% vs 15.7%, P = 0.0017) (Table 1). Among cervical patients, there were no significant differences between POD 0 and POD 1 PT groups regarding approach (anterior, posterior, combined anterior/posterior, p=0.088) or number of levels fused (p=0.3772) (Table 2).

The difference in LOS was statistically significant in both groups, with POD 0 PT patients having shorter LOS. Among lumbar surgery patients, the LOS was 8.9 hours greater for POD 1 PT compared to POD 0 PT (median 65.3 hours for POD 0 PT [interquartile (IQ) range, 43.7-74.6] vs 74.2 hours for POD 1 PT [IQ range 51.6-99.8]; (P < 0.001) (Table 3). Among cervical patients, the LOS was 25.7 hours greater for POD 1 PT compared to POD 0 PT (median 46.8 hours for POD 0 PT [interquartile (IQ) range, 25.7-75.4] vs 72.5 hours for POD 1 PT [IQ range 46.8-101.3], (P < 0.0001) (Table 3). The difference in distribution of postoperative nights spent in the hospital was also statistically significant for lumbar surgery patients (P = 0.002) and cervical patients (P < 0.001) (Table 3). None of the POD 1 PT lumbar patients were discharged on POD 1, while 18.3% of lumbar patients who initiated PT on POD 0 were discharged on POD 1. Among cervical patients, 8.3% of patients who initiated PT on POD 1 were discharged on POD 1, compared to 21.3% of cervical patients who initiated PT on POD 0.

DISCUSSION

As the annual utilization of spine surgery continues to increase, lowering the associated costs remains an important goal as patients and payors demand decreased healthcare expenditures and improved quality. Postoperative LOS is a major factor in the overall costs of cervical and lumbar spine surgery.[13] For medically stable patients, discharge is often dependent on clearance from PT. In our retrospective cohort study of 374 cervical and 336 lumbar patients, we found a significant median difference (25.7 hours for cervical and 8.9 hours for lumbar surgery) in overall LOS and distribution of nights spent in the hospital after surgery (Table 3) in patients who initiated physical therapy on POD 0 vs POD 1. The data suggested no difference between POD PT groups regarding demographics, preoperative ambulation aid use, discharge destination, preoperative myelopathy (for cervical patients), surgical approach or number of levels fused (for cervical patients), which limits concern for confounding variables. Our results demonstrate initiation of PT on POD 0 following >2 level cervical fusion or 1-2 level lumbar laminectomy with or without fusion is associated with decreased postoperative length of stay.

Previous investigations have shown that early postoperative mobilization after orthopaedic surgery may reduce costs, improve outcomes, and shorten postoperative LOS.[12, 14-16] However, much of this literature has focused on total hip arthroplasty and total knee arthroplasty (TKA) patients and the findings have varied. In one prospective cohort study conducted on 136 primary total joint arthroplasties, isolated PT intervention on POD 0 shortened hospital

LOS, regardless of the intervention performed (e.g., ambulation vs moving from bed to chair).[12] A similar study found starting PT on POD 0 was associated with a 1-day decreased LOS with lower pain scores at discharge.[17] However, in another randomized, controlled trial of 394 TKA patients, the authors did not observe a significant difference in hospital LOS or patient satisfaction when PT was initiated on the day of surgery vs the morning after surgery.[18] Although not conclusive, the general trend in orthopaedic literature is that early initiation of PT is associated with decreased length of stay, which is similar to our findings. Despite these findings in similar studies on non-spine orthopaedic patients, there is a lack of information to assess the impact of PT timing on postoperative LOS in spine patients.

Significant variation may exist among different institutions in the delivery, timing, and content of postoperative spine rehabilitation. There are no clear guidelines for patients or providers that describe the best evidence for timing, duration, or content of an optimal postoperative PT regimen. In one study of patient information leaflets from 32 different hospitals that perform lumbar spine surgery in the English National Health Service (NHS), Low et al found significant variations in prescribed frequency and duration of postoperative exercises, descriptions of functional activities, and advice regarding return to normal activity.[19] In another randomized, controlled trial comparing a standard rehabilitation regimen to a fast track rehabilitation regimen for TKA patients, the fast track program patients had a shorter LOS with specific program contents: POD 0 PT, 2 hour daily sessions of PT, group therapy, an organizing case manager, and allowing patients to compare their progress with peers (i.e., "competitive care").[16] In a study of 159 patients undergoing lumbar decompression surgery, Mannion et al found no difference in patient-reported pain or disability between patients who underwent a non-standardized therapy regimen compared to patients whose regimen consisted of specified session frequency, duration, and content of specific isometric exercises according to a published rehabilitation program.[20, 21] The optimal timing, dosage, and content of postoperative PT deserves further investigation, given the impact of rehabilitation quality on recurrent injury, subsequent disability scores, and health care use.[19, 22]

Although the overall length of stay between POD 0 and POD 1 groups differed significantly, over 50% of patients in each group were discharged after 2 or more nights in the hospital, regardless of POD PT timing (Table 3). One explanation of shorter overall LOS for POD 0 patients was that those patients would exhibit greater confidence in subsequent PT sessions, regardless of achievement during the initial session (e.g., getting out of bed to chair vs ambulating in hallway). Initiation of PT on POD 0 may potentially increase patients' self-efficacy in their activity level and their comfort level with PT, thus increasing their progress towards PT discharge clearance in subsequent sessions. While there is limited research on patient's confidence at discharge following spine surgery and physical therapy, previous authors have suggested that patients often complain of a lack of information regarding practical and behavioral recommendations for while at home, which can often be addressed by the physical and occupational therapy teams.[23] It is reasonable to postulate that the earlier that these conversations occur, the earlier a patient may be reassured and more confident in discharging home.

Limitations

Our study subjects were patients from one academic medical center from a single geographic region. Thus, our findings may not be representative of all spine patients in other practice settings and geographic regions. Additionally, we included data from 13 surgeons, who may differ in surgical indications and post-operative algorithms, and we did not control for these differences. Discharge times used for analysis were also based on patients' time of exit from the hospital as logged by the nurse. This time could potentially differ from the actual time they were cleared for discharge by PT if the discharge paperwork process was delayed or the patient was waiting for transportation. However, there were no differences between POD PT groups regarding discharge to a rehabilitation facility (thus requiring waiting for pre-arranged transportation), which could cause such discharge delays.

Our study did not examine postoperative outcomes such as step counts or patient-reported outcomes (e.g., functional score or pain level), and we did not account for patient initiation of activity progression independently or with nursing prior to the first formal PT session (e.g., getting out of bed to chair or hanging the feet over the bedside). Our attributed direct cost per day at inpatient floor status ($724) may not reflect all patients due to variations in care. However, this is the standard calculated value used by our institution's financial analytics department. Other factors besides the timing of PT initiation, including complications (e.g.,

durotomy preventing early mobilization), absence of a home caregiver, or prolonged determination of post-discharge placement by case management. Finally, we did not assess patient reported outcomes and the potential role early PT has on improving objective outcome scores. Further studies should focus on obtaining more generalizable results from multiple practice settings and geographic locations, while accounting for the above-noted limitations through standardization and prospective randomization.

CONCLUSION

There are few studies regarding the association between timing of postoperative PT initiation and postoperative LOS in cervical fusion and lumbar laminectomy patients. Nevertheless, early initiation of PT has been proposed to facilitate earlier discharge following orthopaedic surgery. Our study demonstrated a statistically significant difference in postoperative LOS after cervical or lumbar spine surgery when PT was initiated on POD 0 vs POD 1, suggesting an association between earlier PT and earlier discharge.

Blinded COI Statement: No funds were received in support of this work. No benefits in any form have been or will be received from any commercial party related directly or indirectly to the subject of this manuscript

Disclosures: No funds were received in support of this work. No benefits in any form have been or will be received from any commercial party related directly or indirectly to the subject of this manuscript.

Conflicts of Interest:

- Emily Leary is on the editorial or governing board of JISAKOS and The Journal of Knee Surgery.
- Theodore J. Choma is a board or committee member for AO Spine North America; has stock or stock options with Gentis, Inc.; is a paid consultant for Medtronic Sofamor Danek; is a board or committee member for North American Spine Society; and a board or committee member for the Scoliosis Research Society.
- Don Moore is a board or committee member for AAOS, Lumbar Spine Research Society: Board or committee member and North American Spine Society.
- Daniel W. Hogan, Blaine T. Manning, Suryanshi Rawat, Haley Huff, Shelby Harris, Stefan Hanish, and Nathan Cherian have no other conflicts of interest to disclose.

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	Lumbar POD 0 PT (n=202)	Lumbar POD 1 PT (n=134)	P Value	Cervical POD 0 PT (n=240)	Cervical POD 1 PT (n=134)	P Value
Age (mean ± SD)	57.9 ± 14.4	58.4 ± 14.3	0.66	57.7 ± 11.0	57.8 ± 14.3	0.98
Body mass index (kg/m²; mean ± SD)	33.2 ± 7.8	31.7 ± 5.8	0.23	31.2 ± 7.3	30.4 ± 7.2	0.31
Male Gender (n [%])	92 (45.5%)	70 (52.2%)	0.28	134 (55.8%)	64 (47.8%)	0.16
Insurance: Medicare (n [%])	85 (42.1%)	59 (44.0%)	0.58	97 (40.4%)	64 (47.8%)	0.16
Insurance: Medicaid (n [%])	36 (17.8%)	27 (20.1%)	0.58	39 (16.3%)	26 (19.4%)	0.46
Insurance: Private (n [%])	53 (26.2%)	29 (21.6%)	0.58	73 (30.4%)	21 (15.7%)	0.0017
ASA Classification: 1 or 2 (n [%])	87 (43.1%)	53 (39.6%)	0.58	84 (35.0%)	46 (34.3%)	0.99
Charlson Comorbidity Index (CCI)	1.03 ± 1.12	1.27 ± 1.55	0.56	1.34 ± 1.57	1.43 ± 1.76	0.78
Diabetes (n [%])	49 (24.3%)	31 (23.1%)	0.92	55 (22.9%)	33 (24.6%)	0.81
Preoperative Ambulation Aid (n [%])	37 (18.3%)	17 (12.7%)	0.22	70 (29.2%)	49 (36.8%)	0.17
Preoperative Myelopathy (Cervical only)	n/a	n/a	n/a	142 (59.4%)	85 (63.4%)	0.51
Discharge Destination: Home (n [%])	179 (88.6%)	114 (85.1%)	0.61	195 (81.3%)	96 (71.6%)	0.08

Table 1: Patient Baseline Characteristics, by Postoperative Day PT Group.
POD, postoperative day; PT, physical therapy; ASA, American Society of Anesthesiologists
* Lumbar Patients: n=336
** Cervical Patients: n=374
*Lumbar Patients: elective, inpatient 1-2 level lumbar laminectomy ± posterior lumbar fusion ± instrumentation
**Cervical Patients: inpatient, elective ≥2 level anterior cervical discectomy and instrumented fusion (ACDF) and ≥2 level posterior cervical instrumented fusion +/- laminectomy

Variable	POD 0 PT (n=240)	POD 1 PT (n=134)	P Value
Approach			
Anterior (n [%])	141 (58.8)	72 (53.7)	0.3401
Posterior (n [%])	82 (34.2)	58 (43.3)	0.0817
Combined (Anterior/Posterior) (n [%])	17 (7.0)	4 (2.9)	0.0967
Number of Levels Fused			
2 (n [%])	101 (42.1)	57 (42.5)	0.9402
3 (n [%])	63 (26.3)	36 (26.9)	0.8998
4 (n [%])	48 (20.0)	19 (14.2)	0.1614
5 or more (n [%])	28 (11.7)	22 (16.4)	0.2011

Table 2. Cervical Patient Operative Characteristics, By Postoperative Day PT Group
POD, postoperative day; PT, physical therapy; ASA, American Society of Anesthesiologists
*Inpatient, elective ≥2 level anterior cervical discectomy and instrumented fusion (ACDF) and ≥2 level posterior cervical instrumented fusion +/- laminectomy

REFERENCES

1. Palit M, Schofferman J, Goldthwaite N, et al. Anterior discectomy and fusion for the management of neck pain. Spine (Phila Pa 1976). 1999;24:2224-2228.
2. Buttermann GR. Anterior Cervical Discectomy and Fusion Outcomes over 10 Years: A Prospective Study. Spine (Phila Pa 1976). 2018;43:207-214.
3. Atlas SJ, Keller RB, Robson D, Deyo RA, Singer DE. Surgical and nonsurgical management of lumbar spinal stenosis: four-year outcomes from the maine lumbar spine study. Spine (Phila Pa 1976). 2000;25:556-562.
4. Carreon LY, Glassman SD, Howard J. Fusion and nonsurgical treatment for symptomatic lumbar degenerative disease: a systematic review of Oswestry Disability Index and MOS Short Form-36 outcomes. Spine J. 2008;8:747-755.
5. Liu CY, Zygourakis CC, Yoon S, et al. Trends in Utilization and Cost of Cervical Spine Surgery Using the National Inpatient Sample Database, 2001 to 2013. Spine (Phila Pa 1976). 2017;42:E906-E913.
6. Saifi C, Fein AW, Cazzulino A, et al. Trends in resource utilization and rate of cervical disc arthroplasty and anterior cervical discectomy and fusion throughout the United States from 2006 to 2013. Spine J. 2018;18:1022-1029.
7. Rihn JA, Currier BL, Phillips FM, Glassman SD, Albert TJ. Defining the value of spine care. J Am Acad Orthop Surg. 2013;21:419-426.
8. Sivaganesan A, Wick JB, Chotai S, Cherkesky C, Stephens BF, Devin CJ. Perioperative Protocol for Elective Spine Surgery Is Associated With Reduced Length of Stay and Complications. JAAOS - Journal of the American Academy of Orthopaedic Surgeons. March 1, 2019;27.
9. Naik BI, Dunn LK, Wanchek TN. Incremental Cost-effectiveness Analysis on Length of Stay of an Enhanced Recovery After Spine Surgery Program: A Single-center, Retrospective Cohort Study. Journal of Neurosurgical Anesthesiology. April 2023;35.
10. Danielsen JM, Johnsen R, Kibsgaard SK, Hellevik E. Early aggressive exercise for postoperative rehabilitation after discectomy. Spine (Phila Pa 1976). 2000;25:1015-1020.
11. Nielsen PR, Andreasen J, Asmussen M, Tonnesen H. Costs and quality of life for prehabilitation and early rehabilitation after surgery of the lumbar spine. BMC Health Serv Res. 2008;8:209.
12. Chen AF, Stewart MK, Heyl AE, Klatt BA. Effect of immediate postoperative physical therapy on length of stay for total joint arthroplasty patients. J Arthroplasty. 2012;27:851-856.
13. Gamblin A, Garry JG, Wilde HW, et al. Cost Analysis of Inpatient Rehabilitation after Spinal Injury: A Retrospective Cohort Analysis. Cureus. 2019;11:e5747.
14. Larsen K, Sorensen OG, Hansen TB, Thomsen PB, Soballe K. Accelerated perioperative care and rehabilitation intervention for hip and knee replacement is effective: a randomized clinical trial involving 87 patients with 3 months of follow-up. Acta Orthop. 2008;79:149-159.
15. Larsen K, Hansen TB, Thomsen PB, Christiansen T, Soballe K. Cost-effectiveness of accelerated perioperative care and rehabilitation after total hip and knee arthroplasty. J Bone Joint Surg Am. 2009;91:761-772.
16. den Hertog A, Gliesche K, Timm J, Muhlbauer B, Zebrowski S. Pathway-controlled fast-track rehabilitation after total knee arthroplasty: a randomized prospective clinical study evaluating the recovery pattern, drug consumption, and length of stay. Arch Orthop Trauma Surg. 2012;132:1153-1163.
17. Smith TO, McCabe C, Lister S, Christie SP, Cross J. Rehabilitation implications during the development of the Norwich Enhanced Recovery Programme (NERP) for patients following total knee and total hip arthroplasty. Orthop Traumatol Surg Res. 2012;98:499-505.
18. Bohl DD, Li J, Calkins TE, et al. Physical Therapy on Postoperative Day Zero Following Total Knee Arthroplasty: A Randomized, Controlled Trial of 394 Patients. J Arthroplasty. 2019;34:S173-S177 e171.
19. Low M, Burgess LC, Wainwright TW. A Critical Analysis of the Exercise Prescription and Return to Activity Advice That Is Provided in Patient Information Leaflets Following Lumbar Spine Surgery. Medicina (Kaunas). 2019;55.
20. Mannion AF, Denzler R, Dvorak J, Muntener M, Grob D. A randomised controlled trial of post-operative rehabilitation after surgical decompression of the lumbar spine. Eur Spine J. 2007;16:1101-1117.
21. Richardson CA, Jull GA. Muscle control-pain control. What exercises would you prescribe? Man Ther. 1995;1:2-10.
22. Madera M, Brady J, Deily S, et al. The role of physical therapy and rehabilitation after lumbar fusion surgery for degenerative disease: a systematic review. J Neurosurg Spine. 2017;26:694-704.

23. Ferrari S, Cedraschi C, Mapelli N, et al. Thoughts and concerns of patients at hospital discharge after lumbar spine surgery. A qualitative study. Disability and Rehabilitation. 2023-11-20;45.

ORIGINAL RESEARCH

Rural Residential Status Does Not Impact 1-Year Mortality Rates Following Proximal Femur Fracture Fixation

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ABSTRACT

Background: Proximal femur fractures are a common and serious injury in the geriatric population, often requiring surgical fixation to reduce morbidity and mortality. While previous studies have identified risk factors associated with poor outcomes, the influence of social determinants of health, specifically rural residence and socioeconomic deprivation, remains less clear. Rural patients face unique healthcare access challenges, including longer travel distances and reduced availability of specialized care, potentially affecting outcomes after surgery. Understanding how residential and socioeconomic status influence mortally is essential to improving care for this population.

Objectives: To investigate the relationship between rural residential status and 1-year all-cause mortality rates in geriatric patients following operative fixation of proximal femur fractures.
Methods: A retrospective review was conducted on geriatric patients (≥65 years old) presenting with proximal femur fractures at a midwestern Level 1 trauma center between January 1, 2019, and January 1, 2023. Patient demographics, fracture classification, socioeconomic status (National Area Deprivation Index [ADI] quartile), and residential status (Rural Urban Commuting Area [RUCA]) were collected. Patients were categorized by ADI quartiles and RUCA scores to assess socioeconomic and residential impacts on outcomes. Descriptive statistics were calculated to report means, ranges, standard deviations, and percentages. Demographics were compared between groups, with chi-square or Fisher's exact scores used for categorical variables, and the non-parametric Mann-Whitney U tests used for continuous variables due to lack of data normality. For comparison of continuous variables among ADI quartiles, Kruskal-Wallis tests were used, and Fisher exact tests were used for categorical variables.

Results: 589 patients were included in the RUCA analysis and 577 in the ADI analysis. One-year all-cause mortality was 15.8% (n=94). There was no statistically significant difference in 1-year mortality based on rural, suburban, or urban residential status (p=0.67), nor across quartiles of socioeconomic deprivation measured by Area Deprivation Index (p=0.55). Rural patients were more likely to reside in areas of higher socioeconomic deprivation (p<.001), but this did not impact 1-year survival.

Conclusions: With the increased closure of rural hospitals, rural patients are required to travel greater distanc-

es for orthopaedic care, causing an increased number of rural patients presenting at urban hospitals. The data reported by the current study suggests that rural geriatric patients do not have significantly higher 1-year all-cause mortality rates compared to urban geriatric patients who are operatively treated for proximal femur fractures.

Introduction

Proximal femur fractures contribute to over 500,000 hospitalizations each year, accounting for 26% of orthopaedic fractures in the United States geriatric population.1–3 The mortality rate for nonoperatively managed proximal femur fractures is 46.1% compared to 18.0% for operatively managed patients4, leading to most being managed operatively.5 Several factors are known to be associated with an increased one-year mortality rate including advanced age, medical comorbidities, poor ambulatory status, and male sex.6–10 As surgeons seek to elucidate other factors that make contribute to increased mortality risk, social determinants of health (SDOH) such as measures of neighborhood status and measures of rural status may help identify at-risk patients.

Area Deprivation Index (ADI) scores are a socioeconomic neighborhood measures that take into account 17 unique components from the United States census data to provide a metric of income, education, employment, and housing quality for a given area.11 Previous literature has pointed towards higher levels of socioeconomic deprivation associated with significantly increased risk of mortality at 30, 90, and 365 days following a proximal femur fracture compared to more affluent patients.12,13 However, these studies do not take into account the rural, suburban, or urban status of a patient's home residence. Rural, suburban, or urban residential status is classified based on rural urban commuting areas codes (RUCA), urban influence codes (UIC), metropolitan statistical area (MSA), and rural urban continuum codes (RUCC).14–16 Further, rural hospitals across the United States are closing, limiting access to care for people in these areas by requiring them to travel longer distances to receive care.17,18

To the authors knowledge, no study has investigated the relationship between rural residential status and outcomes following proximal femur fracture fixation. Our hypothesis is that patients living in rural areas have higher 1-year all-cause mortality rates compared to urban patients. The null hypothesis is that there is no difference in mortality rates for patients living in rural areas.

Methods

Data Collection

The current study was reviewed and approved by the institutional review board of the University of Missouri School of Medicine. A retrospective review of all geriatric (>65 years old) patients who presented to a midwestern Level 1 trauma center with a proximal femur fracture and subsequent operative management between January 1, 2019, and January 1, 2023, was completed. Patients were identified through data pulls for international classification of disease (ICD)-9 and ICD-10 codes. ICD-9 codes, 808-808.54, and ICD-10 codes, S32.4-S32.81B, were used for this study. Patient age at time of admission, admission date, discharge date, sex, race, marital status, insurance type, tobacco use status, proximal femur fracture classification, home zip code, discharge location (home, skilled nursing faculty, transfer), American Society of Anesthesiologists (ASA) score, and complications were gathered from the electronic medical record (EMR). Patients who sustained an acetabular fracture or periprosthetic fracture were excluded. Additionally, patients who died during their inpatient stay were excluded.

Area Deprivation Index Scores

ADI scores are used as a numeric proxy for socioeconomic deprivation.19,20 Scores are separated into United States percentiles. United States ADI scores range from 0 to 100.21 Scores near 0 indicate an individual with high socioeconomic standing in society and scores near 100 indicating high levels of socioeconomic deprivation. ADI scores are normalized to the United States population to yield a mean score of 50 with a standard deviation of 10. Patient home addresses are used to calculate US ADI scores. Patients were grouped from US ADI 0-25, 26-50, 51-75, 76-100 for comparison. The grouping of ADI quartiles has been previously described in orthopaedic literature.22–24 The use of national ADI scores for socioeconomic value is well accepted.25–28

Rural Urban Commuting Area Scores

Residential setting is commonly defined using Rural Urban Commuting Area (RUCA) scores by the United States Department of Agriculture based on population density, urbanization, daily commuting, and healthcare access.14 RUCA scores are calculated based on the patients' home zip code. A RUCA score of 1 to 2 indicates

an urban setting, 3 to 5 indicates a suburban setting, and 6 to 10 indicates a rural setting. The use of RUCA scores as a proxy for rural, suburban, and urban status is well accepted.29–31

Statistical Analysis

Descriptive statistics were calculated to report means, ranges, standard deviations, and percentages. Patients were first grouped by survival to discharge, and then by survival at 1-year. Demographics were compared between groups, with chi-square or Fisher's exact scores used for categorical variables, and the non-parametric Mann-Whitney U tests used for continuous variables due to lack of data normality. For comparison of continuous variables among ADI quartiles, Kruskal-Wallis tests were used, and for categorical variables, Fisher exact tests were used. Odds ratios were calculated when significant differences were identified. Significance was set a priori at $p<.05$.

Results

A total of 605 geriatric patients presented to our level 1 trauma center with proximal femur fractures and underwent operative management. Of the 605 patients who were operatively managed, 589 met inclusion criteria for the residential status cohort and 577 met inclusion criteria for the area deprivation index cohort. Five patients were excluded as they did not survive their initial hospital stay, 11 patients did not have information necessary for a RUCA score determination, and 23 patients did not have information necessary for an ADI score determination. (Table 1)

Survival Based on Residential Status

Patients were grouped by living status using RUCA codes to classify them as urban (n=275), rural (n=195), or suburban (n=119). Rural, suburban, and urban patient status was not associated with a difference in 1-year mortality (p=0.67). Rural patients were more likely to live in an area with higher ADI scores compared to suburban and urban patients. No significant differences were identified between rural, suburban, and urban patients in patient's age (p=0.89), tobacco use (p=0.37), length of hospital stay (p=0.24), 1-year survivorship (p=0.67), or fracture type (p=0.62).

Area Deprivation Index Quartiles

Patients with higher ADI scores, indicating greater levels of socioeconomic deprivation, were significantly more likely to live in a rural environment ($p<.001$). There were no significant differences found between ADI quartiles for age (p=0.36), sex (p=0.67), race (p=0.43), marital status (p=0.07), insurance status (p=0.23), length of hospital stay (p=0.50), tobacco use (p=0.65), ASA score (p=0.09), 1-year survivorship (p=0.55), or fracture type (p=0.85). (Table 2)

Patients were grouped by living status using RUCA codes to classify them as urban (n=275), rural (n=195), or suburban (n=119). Rural, suburban, and urban patient status was not associated with difference in 1-year mortality.

Discussion

The results of the current study allow for rejection of the hypothesis that patients undergoing proximal femur fracture fixation and living in rural areas will have higher 1-year all-cause mortality rates compared to urban patients. The current study found that rural patients and urban patients have similar mortality rates of 1-year following proximal femur fracture surgery. Previous literature has reported that rural and urban patients have significantly higher mortality rates among rural patients compared to urban patients at the1-year time point.32,33 The methodology used to classify patients as urban and rural may be contributing to these reported inconsistencies. The aforementioned studies analyzed patients presenting at hospitals designated as urban or rural hospitals. Classifying a hospital as rural or urban does not accurately reflect the patient population it serves. Many rural patients often travel long distances to urban centers for specialized care, such as treatment for complex fractures. As a result, patients from rural areas may be incorrectly categorized as urban simply because they receive care at an urban facility.

Despite previous studies suggesting socioeconomic deprivation is associated with increased postoperative mortality, the current study found no significant association with 1-year mortality and ADI scores.12 A possible explanation for this discrepancy is that the current population was treated at a level-1 trauma center with a dedicated orthopaedic trauma service, which may allow for more comprehensive post-operative care that may negate the negative impact of socioeconomic deprivation. These results suggest that when high quality trauma care is provided to patients, socioeconomic deprivation alone may not be a determining factor for 1-year mortality outcomes for geriatric patients undergoing operative fixation of proximal femur fractures.

As rural hospital continue to close across the United States, there is growing concern for the timely and adequate access to care for rural patients involved in traumatic injuries. As a result, more rural patients are forced to present to urban trauma centers. These hospital closures can result in prolonged transport times, delayed surgical intervention, and challenges in coordinating pre- and post-operative care. Existing trauma centers cover patients from rural or socioeconomic challenged areas should be able to provide adequate post-operative care to allow for patients to heal and return to high levels of physical function.

There are limitations to the current study. This study did not assess outcomes in non-operatively managed patients, which may have different findings compared to operatively managed patients. This study may not account for other factors that could contribute to increased mortality. Future studies should examine other factors, such as mental health status, income, and patient health literacy for impact on mortality.

Conclusion

With the increased closure of rural hospitals, rural patients are required to travel greater distances for orthopaedic care, causing an increased number of rural patients who present to urban hospitals. The data reported by the current study suggests that rural geriatric patients do not have significantly higher 1-year all-cause mortality rates compared to urban geriatric patients who are operatively treated for proximal femur fractures.

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Ethical Statement: The University of Missouri's Institutional Review Board approved this retrospective patient record study.

Author Credit Statement

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Ashwin R. Garlapaty, Alaina C. Bryson, Drew A. Kasten, Harjeev Singh, Kylee Rucinski and Brett D. Crist. The first draft of the manuscript was written by Ashwin R. Garlapaty and Brett D. Crist and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declaration of Interests

The author group has the following disclosures:

Brett D. Crist: Has the following disclosures:

•AO Trauma North America: Board or committee member
•Arthrex, Inc.: Other financial or material support
•Curvafix: Paid consultant; paid presenter or speaker
•DePuy, A Johnson & Johnson Company: Paid presenter or speaker
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•Globus Medical: IP royalties
•International Geriatric Fracture Society: Board or committee member
•Journal of Hip Preservation: Editorial or governing board
•Journal of Orthopaedic Trauma: Editorial or governing board
•Kinetic Concepts, Inc.: Paid consultant; paid presenter or speaker
•Orthocentric: Unpaid consultant
•Orthopaedic Trauma Association: Board or committee member
•RomTech: Stock or stock options
•SLACK Incorporated: Editorial or governing board
•Synthes: Paid consultant; research support
•Urgo Medical: Unpaid consultant

Table 1: Characterization of proximal femur fracture fixation patients based on residential status

Demographic factor	Urban	Suburban	Rural	p-value
Sex				
Male	95	42	56	*p=0.34*
Female	180	77	139	
Age (mean), sd	80.2 (8.56)	79.4 (9.03)	79.9 (8.82)	*p=0.89*
Race				
White	262	116	190	*p=0.26*
Non-white	11	2	3	
Marital status				
Married	112	39	76	*p=0.35*
Single	160	77	116	
Insurance status				
Commercial	14	5	9	*p=0.89*
Medicaid	2	0	0	
Medicare	237	106	175	
Under-insured	22	8	11	
Tobacco use				
Current	34	21	25	*p=0.37*
None	238	98	165	
Length of stay (mean), sd	6.84 (5.77)	7.67 (4.69)	7.45 (6.04)	*p=0.24*
ASA score				
1	0	0	0	
2	50	14	24	*p=0.07*
3	180	90	131	
4	45	13	39	
Survival at 1-Year				
Survived	235	99	161	*p=0.67*
Did not survive	40	20	34	
Fracture classification				
Intertrochanteric	93	50	79	*p=0.62*
Femur	38	19	21	
Head/neck	126	46	83	
Peritrochanteric	8	2	7	
Subtrochanteric	9	2	5	

Key: ASA Score; American Society of Anesthesiologists Score, sd; Standard Deviation

Table 2: Characterization of proximal femur fracture fixation patients based on United States Area Deprivation Index quartiles

Comparisons Based on US ADI Quartiles					
ADI Quartiles, (n)	1	2	3	4	p Value
Number of Patients	6	112	250	209	1.0
Age (sd)	72.8 (7.1)	81.3 (8.2)	80.5 (8.9)	78.6 (8.6)	0.36
Sex					
Male	1	38	86	63	
Female	5	74	164	146	0.67
Race					
White	6	109	243	198	
Other	0	2	5	9	
Unknown	0	1	2	2	0.43
Marital Status					
Single	3	62	145	134	
Married	3	47	104	70	0.07
Insurance Status					
Commercial	0	3	10	14	
Medicaid	0	1	0	0	
Medicare	5	99	227	178	
Uninsured	1	9	13	17	0.23
Length of Hospital Stay					
Day(s) (sd)	4.0 (2.4)	6.8 (6.6)	7.5 (6.3)	7.2 (4.2)	0.50
Tobacco Use					
Yes	0	14	32	33	
No	6	97	217	171	
Unknown	0	1	1	5	0.65
Residential Status					
Urban	6	101	123	40	
Suburban	0	2	51	66	
Rural	0	9	76	103	<.001
ASA Score					
1	0	0	0	0	
2	3	19	28	37	
3	3	74	175	141	
4	0	17	46	31	
5	0	0	0	0	
6	0	0	0	0	0.09
1-Year Survival					
Yes	6	92	206	180	
No	0	20	44	29	0.55
Fracture type					
Intertrochanteric	2	37	95	83	
Proximal Femoral Shaft	1	14	29	33	
Head/neck	3	54	111	81	0.85
Peritrochanteric	0	5	6	6	
Subtrochanteric	0	2	8	6	

Key: ADI; Area Deprivation Index, ASA Score; American Society of Anesthesiologists Score, sd; Standard Deviation

References

1. Brauer CA, Coca-Perraillon M, Cutler DM, Rosen AB. Incidence and Mortality of Hip Fractures in the United States. JAMA. 2009;302(14):1573-1579. doi:10.1001/jama.2009.1462
2. Esper GW, Meltzer-Bruhn AT, Herbosa CG, Ganta A, Egol KA, Konda SR. Defining Characteristics of Middle-Aged and Geriatric Orthopedic Trauma in New York City over a 7-Year Period. Arch Gerontol Geriatr. 2023;112:105039. doi:10.1016/j.archger.2023.105039
3. Keller JM, Sciadini MF, Sinclair E, O'Toole RV. Geriatric trauma: demographics, injuries, and mortality. J Orthop Trauma. 2012;26(9):e161-165. doi:10.1097/BOT.0b013e3182324460
4. Shin ED, Sandhu KP, Wiseley BR, et al. Mortality Rates After Nonoperative Geriatric Hip Fracture Treatment: A Matched Cohort Analysis. J Orthop Trauma. 2023;37(5):237-242. doi:10.1097/BOT.0000000000002549
5. Frenkel Rutenberg T, Assaly A, Vitenberg M, et al. Outcome of non-surgical treatment of proximal femur fractures in the fragile elderly population. Injury. 2019;50(7):1347-1352. doi:10.1016/j.injury.2019.05.022
6. de Haan E, Roukema GR, van Rijckevorsel VAJIM, Kuijper TM, de Jong L, Dutch Hip Fracture RegistryCollaboration. Risk Factors for 30-Days Mortality After Proximal Femoral Fracture Surgery, a Cohort Study. Clin Interv Aging. 2024;19:539-549. doi:10.2147/CIA.S441280
7. Postler A, Posten C, Schubert M, et al. Patients risk for mortality at 90 days after proximal femur fracture - a retrospective study in a tertiary care hospital. BMC Geriatr. 2024;24(1):130. doi:10.1186/s12877-024-04733-8
8. Baghdadi S, Kiyani M, Kalantar SH, et al. Mortality following proximal femoral fractures in elderly patients: a large retrospective cohort study of incidence and risk factors. BMC Musculoskelet Disord. 2023;24(1):693. doi:10.1186/s12891-023-06825-9
9. Bzovsky S, Comeau-Gauthier M, Schemitsch EH, et al. Factors Associated with Mortality After Surgical Management of Femoral Neck Fractures. J Orthop Trauma. 2020;34 Suppl 3:S15-S21. doi:10.1097/BOT.0000000000001937
10. Collin C, Bimou C, Mabit C, Tchalla A, Charissoux JL, Marcheix PS. Orthogeriatric assessment of patients over 75 years of age with a proximal femur fracture: Predictors of 6-month mortality. Orthop Traumatol Surg Res. 2020;106(7):1441-1447. doi:10.1016/j.otsr.2020.06.017
11. Maroko AR. Integrating Social Determinants of Health with Treatment and Prevention: A New Tool to Assess Local Area Deprivation. Prev Chronic Dis. 2016;13. doi:10.5888/pcd13.160221
12. Thorne K, Johansen A, Akbari A, Williams JG, Roberts SE. The impact of social deprivation on mortality following hip fracture in England and Wales: a record linkage study. Osteoporos Int. 2016;27(9):2727-2737. doi:10.1007/s00198-016-3608-5
13. Reyes C, García-Gil M, Elorza JM, et al. Socioeconomic status and its association with the risk of developing hip fractures: a region-wide ecological study. Bone. 2015;73:127-131. doi:10.1016/j.bone.2014.12.019
14. Planey AM, Thomas SR, Friedman H, Hecht HK, Kent E, Holmes GM. Rural Hospital Closures: A Scoping Review of Studies Published Between 1990 and 2020. J Health Care Poor Underserved. 2024;35(2):439-464.
15. Toth M, Holmes M, Van Houtven C, Toles M, Weinberger M, Silberman P. Rural Medicare Beneficiaries Have Fewer Follow-up Visits and Greater Emergency Department Use Postdischarge. Med Care. 2015;53(9):800-808. doi:10.1097/MLR.0000000000000401
16. Powell WR, Sheehy AM, Kind AJH. The Area Deprivation Index Is the Most Scientifically Validated Social Exposome Tool Available for Policies Advancing Health Equity. doi:10.1377/forefront.20230714.676093
17. Patel UJ, Shaikh HJF, Brodell JD, Coon M, Ketz JP, Soin SP. Increased Neighborhood Deprivation Is Associated with Prolonged Hospital Stays After Surgical Fixation of Traumatic Pelvic Ring Injuries. J Bone Joint Surg Am. 2023;105(24):1972-1979. doi:10.2106/JBJS.23.00292
18. Boutrous ML, Tian Y, Brown D, Freeman CA, Smeds MR. Area Deprivation Index Score is Associated with Lower Rates of Long-Term Follow-up after Upper Extremity Vascular Injuries. Ann Vasc Surg. 2021;75:102-108. doi:10.1016/j.avsg.2021.03.037
19. Hassan AM, Nguyen HT, Corkum JP, et al. Area Deprivation Index is Associated with Variation in Quality of Life and Psychosocial Well-being Following Breast Cancer Surgery. Ann Surg Oncol. 2023;30(1):80-87. doi:10.1245/s10434-022-12506-z
20. Johnson AE, Zhu J, Garrard W, et al. Area Deprivation Index and Cardiac Readmissions: Evaluating Risk-Prediction in an Electronic Health Record. J Am Heart Assoc. 2021;10(13):e020466. doi:10.1161/JAHA.120.020466

21. USDA ERS - Rural-Urban Commuting Area Codes. Accessed October 16, 2022. https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx
22. Patel MD, Rosenstrom E, Ivy JS, et al. The Joint Impact of COVID-19 Vaccination and Non-Pharmaceutical Interventions on Infections, Hospitalizations, and Mortality: An Agent-Based Simulation. Published online January 10, 2021:2020.12.30.20248888. doi:10.1101/2020.12.30.20248888
23. Garlapaty AR, Rucinski KJ, Leary E, Cook JL. Do Patients Living in Rural Areas Report Inferior 1-Year Outcomes After Total Knee Arthroplasty? A Matched Cohort Analysis. J Arthroplasty. 2023;38(12):2537-2540. doi:10.1016/j.arth.2023.08.079
24. Garlapaty AR, Sullentrup AN, Christian T, Rucinski K, Crist B. Pre-injury methamphetamine use is associated with increased length of hospital stay in rural orthopaedic trauma patients. Injury. 2024;55(11):111764. doi:10.1016/j.injury.2024.111764
25. Miller BJ, Cai X, Cram P. Mortality Rates are Similar after Hip Fractures for Rural and Urban Patients. Clin Orthop Relat Res. 2012;470(6):1763-1770. doi:10.1007/s11999-011-2140-3
26. Thomas HM, Jarman MP, Mortensen S, et al. The role of geographic disparities in outcomes after orthopaedic trauma surgery. Injury. 2023;54(2):453-460. doi:10.1016/j.injury.2022.11.022
27. Thoors O, Mellner C, Hedström M. Good clinical outcome for the majority of younger patients with hip fractures: a Swedish nationwide study on 905 patients younger than 50 years of age. Acta Orthop. 92(3):292-296. doi:10.1080/17453674.2021.1876996
28. Bergh C, Möller M, Ekelund J, Brisby H. Mortality after Sustaining Skeletal Fractures in Relation to Age. J Clin Med. 2022;11(9):2313. doi:10.3390/jcm11092313
29. Liu E, Killington M, Cameron ID, Li R, Kurrle S, Crotty M. Life expectancy of older people living in aged care facilities after a hip fracture. Sci Rep. 2021;11(1):20266. doi:10.1038/s41598-021-99685-z
30. Bajracharya R, Guralnik JM, Shardell MD, et al. Long-term sex differences in all-cause and infection-specific mortality post hip fracture. J Am Geriatr Soc. 2022;70(7):2107-2114. doi:10.1111/jgs.17800
31. Ceolin C, Bano G, Biz C, et al. Functional autonomy and 12-month mortality in older adults with proximal femoral fractures in an orthogeriatric setting: risk factors and gender differences. Aging Clin Exp Res. 2023;35(5):1063-1071. doi:10.1007/s40520-023-02378-y
32. Lund CA, Møller AM, Wetterslev J, Lundstrøm LH. Organizational factors and long-term mortality after hip fracture surgery. A cohort study of 6143 consecutive patients undergoing hip fracture surgery. PLoS One. 2014;9(6):e99308. doi:10.1371/journal.pone.0099308
33. Ferris H, Merron G, Coughlan T. 1 year mortality after hip fracture in an Irish urban trauma centre. BMC Musculoskelet Disord. 2023;24(1):487. doi:10.1186/s12891-023-06605-5

Ellis Fischel Cancer Center Research Day Abstracts
April 22, 2025

Learning collaborative to reduce tobacco and cancer disparity (LEAD) initiative

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Introduction

Smoking is the leading cause of preventable death, with higher rates among underrepresented populations, including cancer patients. Majorities of individuals who smoke visit a clinician annually and typically desire to quit, although actual treatment delivery remains low. Health organizations and clinicians represent key elements in delivering tobacco treatment. A digital informatics treatment approach can enable care teams to implement evidence-based interventions more efficiently and consistently, ensuring tobacco treatment is integrated seamlessly into routine care. Such an approach removes barriers to treatment, increases the delivery of interventions, ultimately the likelihood of successful smoking cessation and better patient care outcomes.

Methods

The LEAD Initiative launched in fall 2023 between Siteman Cancer Center and the University of Missouri, aims to define and scale tobacco treatment, and is particularly focused on eliminating tobacco-caused rural health disparities in Missouri. Patients expect tobacco to be addressed during health care visits, and consistent interventions are key to improve patient outcomes. Integrating tobacco treatment into routine clinical care using innovative digital informatics has potential to enhance cessation efforts.

Using data from “Informatics for Integrating Biology and the Bedside (i2b2)”, we examined baseline treatment of nicotine dependence of patients of MUHC EFCC from 2018 - 2022. Nicotine dependence prevalence remained high among MU cancer patients (N=24,096-30,157) over the five-year span (2018- 2022, Table), despite a national decline in smoking prevalence. Importantly, we found low rates of tobacco treatment, suggesting a gap in evidence-based treatment and a missed opportunity in cancer management.

Results

Table. MU cancer patients: high tobacco use and low treatment rates	2018	2019	2020	2021	2022
MU patients with >1 cancer dx**	24096	23931	25841	29678	30157
MU cancer patients with nicotine dependence	2852	3017	3269	3509	3497
Prevalence of nicotine dependence	11.8%	12.6%	12.7%	11.8%	11.6%
MU cancer patients with nicotine dependence who received counseling	102	148	118	145	178
Proportion receiving tobacco cessation counseling	3.6%	4.9%	3.6%	4.1%	5.1%

Conclusion

The LEAD intervention will examine additional variables to determine factors contributing to low levels of treatment and health disparities. Further, the future work of LEAD aims to establish a learning health system to evaluate the effect of an evidence-based, low burden smoking module integrated into the MUHC electronic health record workflow to increase tobacco treatment among patients living with cancer. As the project advances in phases, the goal is to ensure tobacco treatment is incorporated into cancer care, as recommended by the National Comprehensive Cancer Network (NCCN) Guidelines, to not only promote smoking cessation, but to improve cancer survival.

A comparison of stereotactic radiosurgery outcomes for brain metastases by primary tumor

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Introduction

Stereotactic radiosurgery (SRS) is a localized radiation therapy used to treat brain metastases. Its effectiveness and safety depend on multiple factors, including the number and size of lesions, which influence treatment parameters such as dosage and fractionation. Another important factor that influences response to treatment is the primary tumor type as some brain tumors are more resistant to treatment than others. Brain metastases originating from lung cancer, breast cancer, and melanoma are more common than those originating from colorectal cancer, ovarian cancer, renal cell carcinoma, esophageal cancer, endometrial cancer, pancreatic cancer, and thyroid cancer. The less common tumors are underrepresented in prior studies and may respond differently to SRS potentially requiring adjusted dose parameters. At our institution, the SRS parameters do not differ depending on the primary tumor type. The aim of this study is to compare survival rates and disease progression between common and rare brain metastases treated with SRS.

Methods

We conducted a retrospective chart review of patients treated with SRS for brain metastases from 2005 to 2023. The primary tumor types were denoted as “rare” and “common” based on how often they are represented in SRS treatments. The rare metastases group included colorectal cancer, ovarian cancer, renal cell carcinoma, esophageal cancer, endometrial cancer, pancreatic cancer, prostate cancer, and thyroid cancer. The common metastases group consisted of lung cancer, breast cancer, and melanoma. Baseline data included primary tumor type and patient age. Outcomes assessed were disease control at 3, 6, and 12 months and survival rates at 6, 12, and 24 months. Chi-square tests were used to analyze survival and disease control rates, while a t-test was used to compare patient age.

Results

A total of 312 patients were included in this study. 260 had common metastases and 46 had rare metastases. The average age of diagnosis for the rare and common groups was 63 and 64 respectively (p=0.483). The rate of brain metastasis control for the rare and common groups was 64.1% and 63.9% (p=0.982) at 3 months, 55.2% vs 63.7% (p=0.382) at 6 months, and 60% vs 51.3% (p=0.469) at 12 months. The survival rate was 76.1% vs 81.9% (p=0.352) at 6 months, 67.4% vs 67.3% (p=0.991) at 12 months, and 58.7% vs 55.4% (p=0.677) at 24 months.

Conclusion

There was no significant difference between the rare metastases and common metastases regarding disease control and survival rate at any time point. The lack of differences in outcomes between the two groups provides evidence that the stereotactic radiosurgery parameters do not need to be adjusted depending on the primary tumor that the brain lesion originated from. Further research into the control of specific lesions depending on the primary tumor type would provide additional valuable insight into this topic.

Temporal trends in survival outcomes following stereotactic radiosurgery for metastatic brain lesions

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Introduction

Stereotactic radiosurgery (SRS) is a key treatment modality for metastatic brain lesions, with technological advancements and evolving treatment strategies potentially improving patient survival over time. Many quality improvement practices and care planning strategies have been implemented to improve outcomes of radiation treatment. This study evaluates temporal trends in survival outcomes for patients treated with SRS at the University of Missouri hospital system over a 25-year period.

Methods

A retrospective chart review was conducted on patients who received SRS as treatment for metastatic brain lesions at the University of Missouri hospital system between 2000 and 2025. Patients were grouped into five cohorts based on their treatment initiation period: 2000–2005, 2006–2010, 2011–2015, 2016–2020, and 2021–2025. Survival at 6, 12, and 24 months post-SRS was recorded and analyzed.

Results

Survival rates following SRS improved over time. For the 2000–2005 cohort, survival at 6, 12, and 24 months was 70%, 40%, and 30%, respectively. In the 2006–2010 group, survival increased to 72%, 52%, and 32%. The 2011–2015 cohort showed further improvement (76%, 64%, 56%), which continued in 2016–2020 (82%, 70%, 57%). The most recent 2021–2025 cohort demonstrated the highest survival rates (83% at 6 months, 76% at 12 months, and 59% at 24 months). However, statistical significance was not observed ($\chi^2 = 1.74$, $p = 0.988$), suggesting that the differences in survival rates across time periods may not be solely attributed to treatment advancements.

Conclusion

While survival following SRS has steadily improved over the past two decades, particularly in long-term survival (24 months), these differences were not statistically significant. The small patient population in earlier cohorts and the presence of multiple confounding factors may have influenced these findings. Further research incorporating larger sample sizes and multivariable analyses is warranted to better understand the specific contributors to improved survival and optimize future treatment strategies.

Incidence and immune profile of myocarditis induced by PD-1 and CTLA-4 inhibition with concurrent radiation

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Introduction

Immune checkpoint inhibitor (ICI) therapy with concurrent radiation has been shown to be a promising treatment for cancers such as non-small cell lung cancer. Current approaches have begun utilizing dual ICI (anti-PD-1/anti-CTLA4) therapy with concurrent radiation to achieve greater responses. However, there has been concern over the potential for life- threatening, cardiovascular complications resulting from this type of treatment. Although prior studies have characterized the incidence and mechanism of cardiotoxicity caused by concurrent PD-1 blockade and radiation, the incidence and mechanism of cardiotoxicity caused by dual ICI therapy with concurrent radiation is still not well understood. The objective of this study is to investigate the incidence and immune profile of myocarditis resulting from anti-PD-1 and anti-CTLA4 therapy with concurrent radiation.

Methods

Eight-to-twelve-week-old A/J mice and C57BL/6 mice were given anti-PD-1 and anti-CTLA4 therapy (dual-ICI), or control antibody via IP injection on Day -1. Half of the mice in both the control and dual-ICI groups were given 20 Gy of radiation on Day 0. Dual-ICI therapy was continuously administered every 3 days to the dual-ICI groups until Day 21. Heart tissue sections were then collected to visualize the presence and severity of ICI-related myocarditis via histology. Heart, spleen, and lymph node tissue, as well as serum, were collected for immune profiling via flow cytometry.

Results

Treatment with anti-PD-1 and anti-CTLA4 therapy with concurrent radiation resulted in a significant incidence of myocarditis, indicated by immune cell infiltration and fibrosis in heart tissue. This effect was greater in A/J mice compared to C57BL/6 mice. The degree of immune infiltrates and fibrosis in heart tissue was used to assess the severity of myocarditis, and greater severity was seen in A/J mice than C56BL/6 mice. Immune profiling of heart tissue infiltrates showed that the predominant immune cells were CD4+ T cells, CD8+ T cells, neutrophils, and macrophages. Autoantibodies specific to cardiac tissues were also found in the sera of mice with cardiotoxicity.

Conclusion

Cardiac-tissue specific autoantibodies were previously found to be a significant driver of cardiotoxicity in mice treated with anti-PD-1 monotherapy and radiation. Additionally, the incidence and severity of myocarditis resulting from dual-ICI therapy with radiation is greater than that of myocarditis resulting from anti-PD-1 monotherapy and radiation. Dual- ICI therapy likely promotes a similar autoantibody-driven mode of pathogenesis to a greater extent. Future studies will further investigate the immune mechanisms responsible for disease pathophysiology with the goal of finding therapeutic approaches to treating concurrent dual-ICI therapy and radiation related myocarditis.

NextGen Precision Health Pathways 2025 Abstracts
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Air pollution, asthma, and educational outcomes: a reflection of systemic racism in the greater St. Louis metropolitan area

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Introduction

Childhood asthma, influenced by environmental factors like air pollution, is a leading cause of student absenteeism, linked to poorer academic outcomes and increased dropout risk. Its prevalence is rising across the U.S., particularly affecting low-income minoritized youth in urban areas. The St. Louis metropolitan area, with its history of segregation and redlining, presents stark racial and socioeconomic disparities, making it an ideal location to assess links between environmental risks, asthma rates, academic outcomes, and socio-demographics.

Methods

This geospatial cross-sectional study utilizes GIS to analyze associations between PM2.5 exposure, childhood asthma ER visit rates, school attendance, third-grade Missouri Assessment Program (MAP) scores, and racial and socioeconomic factors. Statistical analysis via SPSS further explores connections between asthma and academic outcomes.

Results

Findings show PM2.5 emissions exceeding safe thresholds in St. Louis City and North County ($p < 0.001$), areas also exhibiting the highest childhood asthma rates and spatial clustering (Moran's Index 0.576, $p < 0.001$). These areas have lower attendance and MAP scores, particularly in low-income, minority communities exposed to high PM2.5 levels ($p < 0.001$). Academic outcomes also display spatial clustering (Moran's Index > 0.29, $p < 0.001$).

Conclusion

This study highlights the compounded disadvantages faced by racially and socioeconomically minoritized youth in St. Louis, underscoring how environmental injustice perpetuates health and educational inequities, restricting life opportunities for vulnerable youth in the region.

Multi-phase adaptive 4D printed shape memory polymer coils for personalized aneurysm treatment

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Introduction

Aneurysm treatment requires innovative solutions for enhanced safety and efficacy in endovascular procedures. This study introduces a 4D printed dual-transition shape memory polymer coil, using the PGDA-PUA-PAA copolymer, designed for precise aneurysm treatment through its unique multi-phase adaptability and shape recovery onset.

Methods

The PGDA-PUA-PAA copolymer was developed to exhibit dual transition temperatures: Ttrans1 (~20°C) for flexibility during catheter navigation and Ttrans2 (~40°C) for shape memory activation upon deployment. Digital light 4D printing was used to fabricate patient-specific coils deployable through medical catheters. Biocompatibility and functionality were evaluated through in vitro cytocompatibility assays, thrombogenicity tests, and in vivo mouse and rabbit model studies. An in vitro flow model simulated vascular conditions to assess deployment and occlusion capabilities. Mechanical testing analyzed the material's modulus and strain, while histological analyses evaluated tissue integration and inflammatory response.

Results

NMR analysis and spatiotemporal FTIR imaging confirmed the dual transition temperatures and intermediate shape recovery onset. Dynamic Ttrans2 shifted from ~40°C to ~36°C under physiological conditions, enabling onset shape recovery critical for minimally invasive surgery (MIS). The material's modulus transitioned from ~6 MPa (dry) to ~2 MPa (hydrogel), mimicking cardiovascular tissue properties. Dry to Hydrogel transition increases the volume up to 20 times inducing immediate occlusion post-deployment. The strain at failure ranged ~200%, ensuring mechanical stability. Cytocompatibility assays indicated high cell survival, while thrombogenicity tests showed sufficient platelet activation compared to commercial alternatives. In vivo studies demonstrated effective tissue integration with minimal inflammation, and the in vitro flow model confirmed high occlusion rates and adaptability under physiological conditions.

Conclusion

The PGDA-PUA-PAA copolymer offers significant advancements in aneurysm treatment through its dual-transition behavior, intermediate shape recovery onset, and excellent mechanical and biocompatibility properties. These features make it a promising candidate for MIS.

ASICs and their role in controlling pain in the post-operative stage

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Introduction

ASICs are proton-gated cation channels expressed throughout the nervous system that play a role in the modulation of pain and injury in the human body. As they have such a wide variety of functions, it is thought that not only could they be used to modulate pain but also to reduce it. Post-operatively patients often require medication trials that can last from a few days to weeks, and some even devolve into lifelong opioid or pain medication addictions. Due to this, it is highly beneficial to find other ways to manage pain in the postoperative setting without the use of pharmaceuticals, and the manipulation of ASICS can provide just that.

Methods

We conducted a comprehensive literature review using PubMed. The search was limited to English-language articles and included the terms ASIC, acid-sensing ion channels, muscular pain in ASICs, neuropathic pain in ASICs and similar terms. Additional relevant studies were identified by manually reviewing the reference lists of the selected articles.

Results

When studying ASICs, inhibition of particular channels unveils which may be primarily involved in the function of pain. ASIC1 and ASIC3 channels play a significant role in this process. Primary hyperalgesia, pain caused in areas of direct tissue damage, and secondary hyperalgesia, in more distant areas of the damage, can be specifically influenced by these channels. Research involving animals with ASIC1 and ASIC3 channel deficiencies has shown that both primary and secondary hyperalgesia did not develop upon the application of painful stimuli. Other studies revealed that complete blockade of the ASIC3 channel in mice without muscle inflammation has caused inhibition of both primary and secondary hyperalgesia.

Conclusion

ASICs play a crucial role in the regulation and transmission of various signals, including pain. Manipulation of these channels can adequately attenuate pain perception, a key consideration for postoperative care.

Longitudinal assessment of age-related neuromuscular decline in wild type mice

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Introduction

The global population aged 60 and above will double by 2050, underscoring the need to address age-related health declines. Aging is associated with neuromuscular deterioration, reduced strength, and increased disability risk. Recent evidence highlights the critical role of motoneuron deficits and neuromuscular connectivity in weakness, yet these neural contributions remain underexplored. This study investigates the role of motoneuron deficits in age-related neuromuscular decline and their contribution to weakness through longitudinal assessments in wild-type mice.

Methods

Age-related changes in neural excitability and motor function were assessed in 57 C57BL/6J mice (29 females, 28 males) across six age groups: 11-13, 14-16, 17-19, 20-22, 23-25, and 25-27 months. Measurements included compound muscle action potential (CMAP), motor unit number estimation (MUNE), and single motor unit potential (SMUP) to assess neuromuscular excitability, and cervical motor-evoked potentials (cMEP) as a spinal excitability indicator. Motor strength was evaluated using grip strength and weighted cart pull tests.

Results

Both sexes exhibited declines in CMAP starting at 20-22 months compared to 11-13 months. Females showed earlier reductions, at 14-16 months. MUNE showed a significant decline in both sexes at 17-19 months. cMEP amplitudes decreased significantly in both sexes by 14-16 months. While SMUP showed no significant changes, a trend of initial increase followed by later decline was observed. Weight-pulling peaked at 17-19 months before declining at 23-25 months. Grip strength also showed a significant decline in both sexes at 23-25 months.

Conclusion

Age-related neuromuscular decline begins with reduced motor unit connectivity and spinal excitability, leading to later muscle function loss. These findings emphasize neuromuscular mechanisms as key contributors to age-related weakness providing a foundation for future studies, exploring interventions to maintain physical function in aging. Our secondary statistical and molecular analysis will further explore the relationship between neuromuscular integrity and physical function and predictors of decline in aging.

Developing a translational approach to manage dysphagia in ALS patients using optogenetic neuromodulation

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Introduction

Dysphagia, one of the most severe symptoms in ALS patients, increases mortality risk eightfold due to malnutrition and aspiration pneumonia. It initially manifests as tongue weakness, progressing to atrophy and paralysis as hypoglossal motor units (XII MUs) degenerate. There is a pressing need for treatments that delay or halt XII MU degeneration to preserve tongue and swallowing function. We propose optogenetic neuromodulation as a treatment targeting XII MUs with high temporal and spatial resolution. We hypothesize that optogenetics can slow XII MU degeneration, providing a neuroprotective effect on the tongue muscles.

Methods

Using a translational mouse model of ALS (SOD1-G93A), we developed both surgical and non-surgical optogenetic stimulation (opto-stim) protocols for targeted delivery of adeno-associated virus (AAV) mediated excitatory opsin channelrhodopsin (ChR2) into XII MUs. The surgical approach involved stereotaxic injections into the brainstem hypoglossal nucleus (HGN; n=60; 46 SOD1-G93A, 14 littermate controls; either sex) to directly stimulate and record neural activity using a custom-made implantable optrode (optical fiber + electrode). The non-surgical approach involved intramuscular tongue injections (n=11, 4 SOD1-G93A at disease onset, 7 littermate controls; either sex) in lightly anesthetized mice to retrogradely transfect XII Mus.

Results

All SOD1 mice demonstrated robust functional (tongue protrusion via HGN or tongue surface opto-stim) and histological (ChR2 in XII MUs) opsin expression in HGN-injected animals. Intralingual injections (midline injections to the tongue base and blade) evoked tongue surface contractions in anesthetized mice when stimulated with a hand-held optical device. However, results from intralingual injections were suboptimal compared to direct HGN injections.

Conclusion

Our results are promising, demonstrating that the peripheral-based optogenetic stimulation approach was effective in SOD1 mice after clinical disease onset (mirroring ALS onset in humans) with axonal transport deficits. We are currently developing strategies to enhance opsin expression through retrograde transfection to the HGN via intralingual injections.

Trends in global incidence and mortality of colorectal cancer: A 20-year analysis (2000–2020)

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Introduction

Colorectal cancer (CRC) is a significant public health concern and a leading cause of cancer-related deaths worldwide. Advances in screening, diagnosis, and treatment have altered its epidemiology over the past two decades. This study aims to analyze trends in the incidence and mortality rates of CRC globally from 2000 to 2020, focusing on regional differences and associations with healthcare access, economic development, and lifestyle factors.

Methods

A retrospective analysis using data from the Global Cancer Observatory (GCO) and the World Health Organization (WHO) databases. Annual incidence and mortality rates of CRC were collected for 195 countries and adjusted for age. Countries were stratified by income level (low, middle, high) to explore disparities. Correlations between CRC trends and determinants, such as obesity prevalence, dietary habits, and colonoscopy uptake, were evaluated. Linear regression models and joinpoint analysis were employed to identify significant changes in trend slopes.

Results

Between 2000 and 2020, global CRC incidence increased by 20.8%, with the sharpest rises observed in low- and middle-income countries (LMICs) in Asia and Africa. High-income countries (HICs) experienced a 12.4% decline in incidence, attributed to widespread implementation of screening programs and public health interventions. Mortality rates followed a similar pattern: a 15.2% decrease in HICs but a 27.3% increase in LMICs. Obesity and Western-style diets were strongly associated with higher incidence rates in LMICs, while colonoscopy uptake inversely correlated with mortality in HICs ($r = -0.78$, $p < 0.001$).

Conclusion

CRC incidence and mortality have shifted globally over the past two decades, reflecting disparities in healthcare access and lifestyle trends. While HICs demonstrate success in reducing CRC burden through preventive measures, LMICs face rising rates due to limited resources and increasing adoption of risk-associated behaviors.

Socioeconomic disparities in postoperative opioid use following spine surgery: A retrospective analysis of area deprivation index and household income

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Introduction
To investigate the relationship between socioeconomic factors, clinical characteristics, and opioid prescriptions following spine surgery.

Methods
Retrospective cohort study. We conducted a retrospective analysis of 1,132 patients who underwent spine surgery between August 2015 and August 2023. Socioeconomic status was assessed using the Area Deprivation Index (ADI) and household income. The primary outcomes were opioid prescription rates at 3 and 12 months post-surgery. Chi-square tests, t-tests, and Tukey's HSD post-hoc analyses were performed to evaluate associations between socioeconomic factors, clinical characteristics, and opioid prescriptions.

Results
Significant associations were found between 3-month opioid prescriptions and gender ($p=0.0079$), mental health status ($p<0.0001$), fusion status ($p=0.0004$), and procedure type ($p<0.0001$). Males and patients with mental health conditions were more likely to receive prescriptions. While overall household income was not significantly associated with prescriptions ($p=0.9016$), patients in lower income brackets showed higher prescription rates. ADI analysis revealed significant associations in lower to middle percentiles ($p<0.05$). At 12 months, these associations were less pronounced. Preoperative narcotic use ($p<0.0001$) and complex procedures were associated with higher prescription rates at both time points. 15.52% of patients received prescriptions at both 3 and 12 months.

Conclusion
Socioeconomic factors and clinical characteristics influence short-term postoperative opioid use following spine surgery, but their impact on long-term use is less pronounced. These findings highlight the need for targeted interventions in the early postoperative period and comprehensive, individualized approaches to long-term pain management that address the complex interplay of socioeconomic, clinical, and patient-specific factors.

Understanding host-pathogen dynamics using model-based hypothesis testing: A mathematical framework

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Introduction
Disease models have traditionally been used to understand the dynamics of infectious diseases and evaluate the effectiveness of various interventions or policies for control and prevention. However, their capability for testing epidemiological hypotheses about the ecology and evolution of pathogens remains underexplored. Objectives: This study aims to highlight the potential of disease models to test competing epidemiological hypotheses using a novel approach called Model-Based Hypothesis Testing (MBHT). The focus is understanding the interplay between pathogen evolution and public health interventions.

Methods
A compartmental disease model was developed and parameterized using U.S. COVID-19 infected data from seven epidemic waves. Six hypotheses were tested using the Bayesian inference approach: (H1) Transmission-Virulence Trade-Off, (H2) Short-Sighted Evolution, (H3) Vaccination-Induced Virulence, (H4) Immune Selection, (H5) The Law of Declining Virulence, and (H6) Transmission-Virulence Correlation. Simulations were conducted to evaluate changes in the reproduction number (R0) and posterior probabilities of the hypotheses across epidemic waves.

Results
The probabilities of the hypotheses varied across epidemic waves. Early waves were dominated by H1 and H2, indicating a balance between transmission and virulence and the pathogen's focus on immediate fitness advantages. Immune Selection (H4) became the dominant hypothesis in mid-waves, driven by mutations enhancing immune escape. In later waves, The Law of Declining Virulence (H5) emerged as the most probable hypothesis, aligning with reduced severity observed in newer variants of SARS-COV-2.

Conclusion
This study demonstrates the utility of MBHT in hypothesis testing, providing a robust framework for understanding the evolution of infectious diseases. The findings emphasize the dynamic interaction between pathogen adaptation and public health interventions, offering insights into selective pressures shaping epidemic dynamics and guiding future public health strategies.

Exploring end-user preferences for AI-assisted behavioral pain interventions

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Introduction

Chronic pain remains a significant public health issue affecting 21% of the U.S. population, leading to impaired physical, cognitive, and emotional functioning. Behavioral pain interventions activating the lymphatic system effectively manage pain through multimodal strategies such as therapeutic lymphatic exercises, healthy diets, and proper sleep. AI can assist in delivery of personalized behavioral pain intervention through precision training, providing real-time tailored recommendations, and tracking effectiveness of lymphatic exercises. This study explores adult end users' perspectives on AI-assisted behavioral pain interventions and evaluates their intentions to use and willingness to pay.

Methods

A cross-sectional design was used to recruit 30 adults with pain history. Participants were trained to perform lymphatic exercises while imagining AI-assisted support (e.g., real-time tracking or feedback). Data were collected on demographics, preferences for behavioral pain interventions, intentions to use and willingness to pay for AI-assisted solutions. Descriptive and inferential statistics were used for analysis.

Results

Participants were from diverse backgrounds (30% Asian, 13.33% Hispanic, 33.33% Black, 33.33% White), genders (43.33% Male, 56.67% Female), and ages (Mean: 34.33, SD: 13.94, Range: 18-69). All participants found lymphatic exercises effective, with 93.33% rating them as "quite" to "very helpful." Black participants showed significantly higher acceptance of AI-assisted solutions ($W = 53$, $p = 0.0217$). Participants expressed strong intention to use AI-assisted devices (average rating: 8.13/10) and preferred mobile phones (83.33%) for such programs. Notably, 56.67% were willing to pay $20/month for the system.

Conclusion

The study highlights participants' acceptance of and preferences for AI-assisted behavioral pain interventions, including their strong intention to use and their willingness to pay for them. Insights into preferred devices and AI features (e.g., personalized pain management and real-time tracking) emphasize the readiness to integrate AI into behavioral pain interventions. These findings are vital for co-designing effective and user-friendly AI-assisted systems to manage chronic pain.

Determining the effects of race on pancreatic neuroendocrine cancer patient diagnosis and outcomes

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Introduction

To investigate the influence of race on patient outcomes in pancreatic neuroendocrine tumors (PNETs), specifically examining overall survival, primary tumor location, histopathological grade, tumor size, and patterns of metastatic organ dissemination.

Methods

A retrospective cohort analysis was conducted on PNET cases stratified by race. Kaplan-Meier survival models were used to examine racial differences in survival, while multivariable Cox proportional hazards regression adjusted for confounding variables. Chi-square and ANOVA tests were used to assess associations between race and tumor characteristics (primary site, grade, size, metastasis). Metastatic involvement in bone, brain, liver, and lung was also evaluated. A significance threshold of $p < 0.05$ was applied.

Results

Race was proven to be an independent survival predictor, with non-Hispanic Non-Hispanic Black patients more likely to have tumors in the pancreatic tail ($p < 0.001$), a site associated with poorer outcomes. Hispanic patients had a higher frequency of poorly differentiated tumors ($p = 0.001$), while non-Hispanic Asian or Pacific Islander patients presented with larger tumors (mean size 4.3 cm vs. 2.8 cm, $p = 0.003$). Non-Hispanic Whites were more prone to liver metastasis ($p < 0.001$), while bone metastasis was more common in Hispanic patients ($p = 0.032$).

Conclusion

Non-Hispanic Black and Hispanic patients have more aggressive PNET characteristics, larger tumors, and poorer survival outcomes. Racial differences in metastatic spread, particularly the higher rates of liver metastasis in non-Hispanic Whites and bone metastasis in Hispanics, suggest that biological or healthcare access disparities influence disease progression. Further research should focus on integrating genomic, proteomic, and healthcare access data to better understand these disparities and guide personalized treatment approaches.

RNNs for seizure onset zone (SOZ) mapping: Data-driven solutions in epilepsy

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Introduction

Patients with drug-resistant epilepsy have uncontrolled seizures while taking medications. A clinical problem is locating the cortical region causing seizures, called the seizure onset zone (SOZ), to either surgically resect or stimulate it. This project uses cortico-cortical evoked potentials (CCEPs) and a machine learning model to predict the SOZ location. The goal is to improve SOZ identification accuracy to aid clinical decision-making.

Methods

We reanalyzed a published CCEP dataset from 7 patients with focal epilepsy who underwent intracranial electrode placement for seizure monitoring. CCEP data were collected by stimulating brain channels and recording responses across other electrodes as a measure of brain connectivity. Among the channels stimulated were those thought to be in the SOZ. The CCEP data were used to train a recurrent neural network (RNN) with long short-term memory (LSTM) layers to classify SOZ status. The dataset was split into 70% training, 15% validation, and 15% testing, with learning rate scheduling and early stopping to prevent overfitting. Temporal features, such as trial and power data, were normalized and padded for consistency. The architecture includes two LSTM layers, dropout layers, and fully connected layers for classification.

Results

The model achieved a training accuracy of 89.21%, validation accuracy of 78.69%, and testing accuracy of 85.08%. It had a precision of 0.71, recall of 0.72, and F1 score of 0.71. The confusion matrix showed 358 true positives (SOZ) and 1335 true negatives (non-SOZ). The AUC-ROC curve was 0.892, indicating strong performance.

Conclusion

This RNN-based model can predict which electrodes were part of the patient's SOZ and thus may be a candidate for surgical resection. This may help guide epileptologists' treatment plan for patients with focal epilepsy. Ongoing improvements aim to refine the model and validate its use in diverse patient groups.

Lorcaserin Administration Increases Motor Function in Aged Mice

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Introduction

Sarcopenia, age-related decline in muscle mass and strength, reduces independence and increases all-cause mortality. Our research suggests increasing motoneuron excitability via lorcaserin, a specific 5-HT2c agonist, can improve muscle function in aged mice. Here we sought investigate the impact of chronic lorcaserin treatment on motor function in aged mice.

Methods

At baseline, aged mice (20-month-old, n=16, 50% female) underwent behavioral assessments of muscle function (all-limb grip, rotarod, and the weighted cart pull (WCP) with average power estimation) and in vivo electrophysiology and muscle contractility. Mice were randomized to daily treatments (3 mg/kg lorcaserin or saline) by oral gavage 2 hours before dark (12h-12h light-dark cycle) for 3 weeks. After, mice were retested in two conditions: 1) 1 hour after treatment to assess predicted peak drug level (PP) and 2) 18 hours after treatment to assess predicted trough (PT) drug level. All behavioral assessments occurred at the same time of day.

Results

Lorcaserin-treated mice show an improvement in the average power with testing occurring at PT time compared to baseline but not at PP. Lorcaserin-treated mice at PT show a negative correlation with baseline cMEP/CMAP (an index of spinal motor neuron excitability), while saline-treated mice show a positive correlation with baseline cMEP/CMAP.

Conclusion

Chronic lorcaserin treatment improves motor function in aged mice, particularly at the PT time point. These effects were not observed at PP. We hypothesize that this variability may be related to the oral gavage delivery that occurs 1 hour prior to PP testing, but alternatively these findings could suggest a need for continued optimization of the dosing intervention. The negative correlation between motor performance and cMEP/CMAP indicates that lorcaserin benefits mice with spinal motor neuron hypoexcitability. Further research is needed to explore the long-term effects on neural function, excitability, and body composition.

Examining equity in academic performance among underrepresented students in health sciences

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Introduction

The Students Training, in Academia, Health, and Research (STAHR) Program at UMKC aims to increase the number of students from economically or educationally disadvantaged backgrounds who succeed in health sciences degree programs. This study examines achievement equity in the STAHR Program, focusing on social and environmental factors contributing to achievement, with implications for addressing disparities in health sciences education and improving program support for underrepresented students.

Methods

Cumulative GPA data for STAHR students from Spring 2018 to Fall 2022 were collected from UMKC's Registrar and compared to non-STAHR students' GPAs. Demographic information from STAHR Program applications was merged with GPA data for analysis. Institutional Review Board (IRB) approval was obtained for the program evaluation. Multilevel modeling was used for the analysis.

Results

Racial and ethnic background influenced academic performance. African American/Black students had lower GPAs in Medicine and Dentistry, but higher GPAs in Pharmacy compared to white students. Asian students tended to have higher GPAs in Medicine and Pharmacy. Hispanic/Latino students in Medicine had lower GPAs, while those in Pharmacy had higher GPAs. Female students generally performed better than male students in Medicine.

Conclusion

STAHR students performed comparably to, and in some cases outperformed, non-STAHR students, particularly in the Undergraduate Medicine Program. This success is notable given that many STAHR students lacked prior clinical or professional experience. The program's mentorship, workshops, and peer support contributed to this achievement. Minority students, especially African American/Black students, benefited from STAHR support, performing similarly to white students. The program has implemented strategies like matching students with mentors from similar backgrounds and partnering with community clinics to enhance exposure. Future research will refine demographic comparisons and explore factors impacting achievement, including in subgroups like Black students.

A de novo mutation in synaptotagmin-1 induces neurological disorders

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Objective

Mutation in a calcium-binding domain of synaptotagmin 1 (SYT1), which is a presynaptic calcium sensor, in patient-induced SYT1-associated neurodevelopmental disorder (SYT1-NDD). A de novo mutation in SYT1 has been identified in patients with neurological disorders. This study aims to establish and validate mouse models carrying this SYT1 mutation, which will be used to test therapeutic approaches.

Methods

A mixture of adeno-associated viral (AAV) vectors containing Cre-dependent mutant Syt1 (AAV9-FLEX-CMV-Syt1 D365E-P2A-EGFP) and AAV-CMV-Cre was infused into the mouse hippocampus. AAV9-CMV-EGFP vector was used as a control. Behavioral tests were performed including an elevated plus maze, open field exploration, 3-chamber test, novel objective recognition, and rotor rod tests.

Results

Mice with AAV-mediated expression of mutant SYT1 in the hippocampus displayed impaired sociability and social novelty in the 3-chamber test, compared to mice with only GFP expression in the hippocampus. The behaviors including total activity, anxiety level, cognitive function, and motor function performed in mice with mutant SYT1 expression did not differ from mice with GFP expression.

Conclusion

These data suggest that mutant SYT1 in the hippocampus induces autism-like behavior. This AAV-mediated expression of mutant SYT1 in a mouse model is a promising model for testing future therapeutic approaches.

Cholinergic interneurons in the accumbal shell region regulate binge alcohol self-administration in mice: An in vivo calcium imaging study

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Objective

The study investigates the relationship between binge alcohol consumption and the activity of cholinergic interneurons (CIN) in the nucleus accumbens shell (NAcSh) using real-time in vivo calcium imaging. We hypothesize that binge drinking increases CIN activity in the NAcSh, contributing to alcohol self-administration behaviors.

Methods

Male transgenic mice expressing Cre-recombinase in cholinergic neurons were exposed to the Drinking in the Dark (DID) paradigm, a validated model for binge drinking. Mice in the alcohol group consumed 20% (v/v)alcohol, while the control group consumed 10% (w/v) sucrose. Calcium imaging was conducted using a microendoscopic technique to monitor CIN activity in real-time. Discharge activity was measured using calcium transients, including frequency and amplitude, during alcohol and sucrose consumption.

Results

Mice exposed to alcohol displayed significantly higher frequencies and amplitudes of CIN discharge activity compared to the sucrose group. This heightened activity was measured using calcium transients, demonstrating a marked increase in both groups but notably more pronounced during alcohol consumption. These results suggest that CIN activity in the NAcSh correlates strongly with alcohol self-administration behaviors.

Conclusion

The study reveals a crucial link between CIN activity in the NAcSh and binge alcohol consumption. The findings highlight the potential of targeting CIN activity as a therapeutic strategy for addressing alcohol use disorders (AUD). By elucidating the neurobiological mechanisms underlying binge drinking, this research contributes to the development of more effective interventions for AUD.

Bruno1 isoforms have distinct subcellular localization patterns in developing indirect flight muscle of drosophila

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Introduction

Bruno1 (Bru1) is a conserved member of the CELF family of RNA binding proteins, which are key regulators of alternative splicing and muscle development from flies to vertebrates. CELF1 is misregulated adult patients with myotonic dystrophy type 1 (DM1), and in flies, Bru1 instructs a developmental transition to mature splice isoforms in indirect flight muscle (IFM), as well as sarcomere growth and myosin contractility. Bru1 itself undergoes alternative splicing to produce at least 11 transcripts and 6 distinct proteins, and here we test if different splice isoforms of Bru1 have distinct subcellular localization patterns and functions.

Methods

We examined the subcellular localization of an endogenously tagged Bru1eGFP protein, as well as individual GFP-tagged Bru1 isoforms, using confocal microscopy. Using immunofluorescence, we examine Bru1 localization across IFM development and test if PKA activity is necessary for the nuclear localization of Bru1.

Results

Our results show that during early stages of IFM development, Bru1eGFP is localized in discrete granules in the cytoplasm as well as in nuclei. As the IFM matures, Bru1eGFP progressively translocates and becomes enriched in the nucleus. This indicates that Bru1 may have a cytoplasmic function during early myogenesis, but is likely predominantly involved in regulating alternative splicing during muscle maturation. Using UAS-GFP-Bru1 constructs, we find isoform-specific patterns of subcellular localization in IFM. CELF proteins in vertebrates are known to shuttle between the cytoplasm and nucleus due to PKA-mediated phosphorylation, and we test if Bru1 nuclear localization in IFM is PKA-dependent, using RNAi knockdown and overexpression to modulate PKA activity.

Conclusion

Our results implicate regulation of Bru1 protein localization as a mechanism to regulate CELF-protein activity. Further, we provide the first evidence that different Bru1 isoforms may play distinct roles during muscle development, providing another mechanism to fine-tune CELF activity.

Mechanisms of NF-κB signaling in development of lung-tissue resident memory T-cells

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Objective

The NF-kB pathway is crucial for forming and maintaining tissue-resident memory Tcells (TRM), which are essential for long-term immunity against respiratory pathogens. We previously demonstrated that increasing NF-kB signaling in CD8+ T cells late in the immune response results in a loss of influenza-specific lung CD8+ TRM cells and impaired protective immunity against re-infection. Conversely, decreasing NF-KB signaling during the same phase of the immune response enhances the generation of influenza-specific CD+ TRM in the lungs. In this study, we investigated whether decreasing NF-B signaling improves protective immunity against re-infection. Understanding NF-kB's role in protective immunity is significant, as it could aid in developing new therapies to improve lung immunity against rapidly mutating viruses like influenza and SARS-CoV-2.

Methods

We generated novel T cell-restricted inducible tetON IKK2 mouse models, allowing for the controlled reduction of IKK2/NF-kB signaling in T cells during specific phases of the immune response via doxycycline exposure. Using different influenza A virus (IAV) strains, we assessed the level of heterosubtypic protective immunity conferred by inhibiting NF-B signaling 10-30 days post-infection (dpi). Transgenic tetON mice carrying a dead IKK2 kinase inducible transgene and control littermates were infected with IAV/X31 and treated with doxycycline chow from 10-30dpi to decrease NF-kB signaling. At 30dpi, the cohorts were divided: one group was sacrificed to assess influenza-specific lung TRM levels, while the other was re-infected with a lethal dose of heterosubtypic IAV/PR8, with weight loss monitored for 15 days.

Results

Inhibition of NF-kB during memory T cell formation significantly improved TRM- mediated protection, as shown by reduced weight loss after IAV/PR$ challenge, indicating enhanced heterosubtypic immunity.

Conclusion

Inhibiting NF-B signaling late in the response enhances TRM-mediated immunity against heterosubtypic influenza infection. These results suggest that targeting NF-KB could improve vaccine-induced immunity and reduce disease severity upon re-infection.

Uncommon presentation of histoplasmosis: A case of migratory polyarthritis in an immunocompetent patient

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Introduction

To describe a rare case of histoplasmosis presenting as migratory polyarthritis in an immunocompetent patient and to emphasize the importance of including fungal infections in the differential diagnosis of polyarthritis, even in individuals without apparent immunosuppression.

Methods

This case report discusses the clinical presentation, diagnostic evaluation, and management of a 32-year-old immunocompetent male who presented with migratory polyarthritis. Diagnostic workup included serological testing, imaging, and a lymph node biopsy. The differential diagnosis initially considered autoimmune, infectious, and inflammatory causes, and the case was complicated by a positive T-spot TB test. Histoplasmosis was ultimately confirmed through serological testing following biopsy results.

Results

The patient presented with migratory polyarthritis and lacked typical respiratory symptoms associated with histoplasmosis. Initial diagnostic tests, including arthrocentesis and serologies for autoimmune and infectious conditions, were inconclusive. Imaging studies identified hilar adenopathy, leading to a differential including sarcoidosis and tuberculosis arthritis. Despite a positive T-spot TB test, acid-fast bacilli stains were negative. Lymph node biopsy revealed necrotizing granuloma, strongly suggestive of histoplasmosis, later confirmed by serological testing. The patient was successfully treated with itraconazole, with significant symptom resolution observed within weeks.

Conclusion

This case highlights the diagnostic complexity of histoplasmosis presenting as migratory polyarthritis in an immunocompetent patient. The findings underscore the need for a broad differential diagnosis when evaluating polyarthritis, including fungal infections, especially in endemic regions. Clinicians should maintain a high index of suspicion for histoplasmosis even in patients without classic respiratory or systemic symptoms. Recognition of histoplasmosis as a potential cause of polyarthritis

Histone deacetylase inhibitor, trichostatin a (TSA) enhances triple negative breast cancer oncolytic virotherapy

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Objective
Determine the ability of histone deacetylase inhibitor (HDACi), Trichostatin A (TSA) to enhance triple-negative breast cancer (TNBC) oncolytic virotherapy in vitro.

Methods
Human TNBC MDA-MB-231, HCC1937, and MDA-MB-157 were infected at increasing multiplicity of infection (MOI) concentration with a replication-defective adenovirus (Ad) expressing green fluorescent protein (AdGFP) (non-oncolytic virus as a control) or an oncolytic Ad (OAd) expressing the reporter red fluorescent protein mCherry (OAdmCherry) on the virus capsid. TNBC cells were also treated with at increasing concentrations of Trichostatin A (TSA). At 72 h post-infection or TSA treatment cell viability was evaluated by alamarBlue assay and IC50 values were then determined for each individual agent.

Results
TNBC cells were treated at increasing concentrations of TSA followed by AdGFP infection, at 24 h post-infection GFP expression was assessed by fluorescent microscopy. It was found that the number of GFP positive cells increased in a TSA dose-dependent manner, suggesting that TSA enhances virus infectivity. This was further validated by the increased expression of coxsackie adenovirus receptor (CAR). Next, TNBC cells were pretreated with TSA followed by OAdmCherry using the IC50 values to create a combined treatment that can increase viral potency and oncolysis. The combined therapy of OAdmCherry + TSA displayed greater number of red-positive cells than OAdmCherry-infected cells alone and oncolytic cell death was also greater than each agent alone.

Conclusion
The results suggest that TSA enhances TNBC oncolytic virotherapy which may depict a possible alternative approach to destroy TNBC tumors in patients. The combined therapy of OAdmCherry + TSA displayed a greater killing effect than each agent alone. The increased killing effect was at least in part due to increased infectivity and replication. This therapeutic regimen remains to be evaluated in a preclinical mouse model of TNBC.

Profiling age-related loss of motor function: Corticospinal excitability, a major contributor to weakness?

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Objective
Aging impairs physical function, leading to loss of independence and increased morbidity. Motor function relies on coordinated activity of the central nervous system (CNS), peripheral nervous system (PNS), and skeletal muscle. While sarcopenia has traditionally been viewed as a muscle-centric issue, emerging evidence highlights neurological impairments as key contributors. The impacts of chronological aging vary among individuals, as biological age often differs from chronological age. This study examines CNS, PNS, and skeletal muscle function, focusing on the variability of biological aging in neuromuscular function using C57BL/6 mice.

Methods
Young and aged (3-4, 24-26 months) mice underwent motor performance (grip and maximum weight cart pull), muscle contractile, and electrophysiological [compound muscle action potential (CMAP), single motor unit potential (SMUP), motor unit number estimation (MUNE), and cervical motor evoked potential (cMEP)] testing. Based on motor performance, aged mice were classified into frail or resilient groups (n=8 each), with a young control group (n=8) for comparison. Spinal cord tissues were collected, and single-nuclei RNA sequencing was performed.

Results
Aged mice showed declines in motor strength, power, and torque, with increased fatigue. Electrophysiological tests revealed reduced CMAP, MUNE, and cMEP, indicating impaired motor unit connectivity and CNS excitability, while SMUP increased, suggesting compensatory sprouting. cMEP had the strongest association with motor function, correlating with grip strength and cart pulling. Our sequencing data showed high quality and gene diversity, with 94% of reads mapping to the genome and 50% to intronic regions.

Conclusion
Comprehensive evaluations in aged mice demonstrated impairments across CNS, PNS, and muscle systems. Strong correlation between cMEP and motor function highlights corticospinal excitability as a potential therapeutic target to counteract age-related physical decline. Ongoing snRNA-seq analysis will investigate differential gene expression between resilient and frail mice, offering insights to understand and mitigate frailty.

Designing PISA-based 3D printable resins for resorbable tissue engineering scaffolds

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Objective
To develop a novel 3D printing approach utilizing Polymer-Induced Self Assembly (PISA) with difunctional macro chain transfer agents (macro-CTAs) to produce mechanically stable, physically crosslinked objects without the need for chemical crosslinkers, enabling controlled dissolution and potential applications in tissue engineering.

Methods
A difunctional polyethylene glycol (PEG) macro-CTA was synthesized and chain-extended with diacetone acrylamide (DAAm) in water. The resulting PISA resin was 3D printed using digital light projection (DLP) with lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) as the photoinitiator and phenol red as the photoabsorber. Resins were printed both with and without 2.5 wt.% N,N'-methylenebisacrylamide (MBAc) chemical crosslinker. The printed objects were characterized using atomic force microscopy (AFM) and scanning electron microscopy (SEM) to assess their nanostructures and microstructures. Mechanical properties were evaluated through tensile testing of molded dogbone samples.

Results
Both crosslinked and uncrosslinked DAAm PISA resins produced satisfactory 3D prints that maintained their shape. The uncrosslinked parts were insoluble in water but dissolved completely in N,N-dimethylformamide (DMF), confirming the absence of chemical crosslinks and the presence of physical crosslinking. AFM images revealed worm-like particles and phase-separated domains, indicating successful self-assembly during the printing process. SEM imaging showed a vasculature-like porous network within the printed objects. Mechanical testing demonstrated that uncrosslinked parts had high elasticity and elongation due to physical crosslinks, while crosslinked parts were stiffer with reduced elongation. Controlled dissolution experiments showed that specific parts of a composite structure could be selectively dissolved, highlighting the ability to manipulate the solubility and integrity of the printed objects.

Conclusion
The study successfully demonstrates that PISA can be integrated into 3D printing to create physically crosslinked, mechanically stable objects without chemical crosslinkers. This method allows for controlled dissolution and the formation of unique nanostructures and microstructures, such as vascular.

Weighted cart pull with an average power estimation: Developing a novel outcome measure for motor function in mice

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Objective

Sarcopenia, the pathological age-related decline in muscle mass and strength, is a contributor to impaired independence and quality of life in older adults. Effective treatments are lacking, and robust preclinical models are needed to advance translational research. This study aimed to develop and validate the Weighted Cart Pull (WCP) as an assessment of muscle function in aged mice.

Methods

The WCP test involved attaching a weighted cart to the tail of mice as they ascended a ramp to a resting area. Weight was incrementally increased until failure, defined as either five consecutive hindquarter taps without progress or sliding backward. Following failure, a timed trial with 50% of the maximum pull was performed to estimate average power. Young (7 months, n=10) and old (25 months, n=10) mice underwent WCP, grip strength, and rotarod tests. In vivo electrophysiology and muscle physiology were measured to correlate WCP results with traditional assessments. Additionally, a cohort of 9- and 25-month-old mice was tested to evaluate WCP intra- and inter-rater reliability.

Results

Seven-month-old mice pulled significantly more weight than 25-month-old mice ($p=0.0001$). WCP outcomes correlated with grip strength ($r=0.6481$, $p=0.0027$) and rotarod performance ($r=0.6332$, $p=0.0036$). Average power correlated with grip strength ($r=0.5883$, $p=0.0081$). WCP also correlated with single motor unit potential ($r=-0.6632$, $p=0.0020$), motor unit number estimation ($r=0.5146$, $p=0.0242$), neuromuscular transmission during repetitive nerve stimulation ($r=0.4673$, $p=0.0437$), and tetanic torque ($r=0.4915$, $p=0.0326$). Average power correlated significantly with compound muscle action potential ($r=0.4823$, $p=0.0365$) and other electrophysiologic measures. Intra-rater reliability was excellent (ICC=0.735, $p<0.0001$), while inter-rater reliability was moderate (ICC=0.427, $p=0.0509$).

Conclusion

The WCP and average power assays provide robust, cost-effective methods for assessing motor function, strength, and power in mice. This tool enhances preclinical evaluations and holds promise for characterizing disease models and testing therapeutic interventions.

Patient understanding of the resident physician's role in Orthopaedics

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Objective
Academic hospitals play a crucial role in the U.S. healthcare system, frequently hosting resident physicians who are integral to patient care. Despite this, patients do not always well understand the role of resident physicians.

Methods
We conducted a prospective survey of 159 orthopedic patients at an academic sports medicine clinic from April 2023 to August 2024 to assess their understanding of the resident physician's role. In addition to demographic information, the survey included a knowledge-based questionnaire designed to evaluate patients' awareness of the responsibilities and qualifications of resident physicians.

Results
The mean age of respondents was 43.6 years, with 57.1% being female and 85.1% of white ethnicity. Education levels were evenly distributed across graduate degrees (19.3%), college degrees (37.9%), and high school diplomas (39.1%). Most patients (77.7%) correctly identified a resident as a doctor, with this figure increasing to 86% when additional context was provided. Notably, 93.6% of patients understood that residents must be supervised by an attending physician, a figure that increased to 94.9% for surgical settings.

Conclusion
Our findings suggest a moderate to high level of patient awareness regarding the qualifications and role of resident physicians. However, nearly one in five patients still need more clarity on this issue, underscoring the need for ongoing educational efforts. Notably, improvements in patient understanding of supervision requirements suggest that enhanced communication and educational strategies have had a positive impact over the past decade.

Jujube is a potential powerful treatment for melanoma by upregulation of p21, p53, and TRAILR1

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Objective
Malignant melanoma is the deadliest skin neoplasm. Approximately 100,640 new cases are expected to be diagnosed in the United States in 2024. Ziziphus jujube (jujube) has been used in Chinese herbal medicinal practices for thousands of years. Recently, jujube has been studied for its anti-cancer properties in some cancer, however, its role and mechanisms in melanoma are not well understood. This study was designed to investigate the direct effects of jujube on melanoma and its possible molecular mechanisms.

Methods
Clonogenic survival assay, cell proliferation, TUNEL and caspase-3 activity kits were used to evaluate the effects jujube on cell survival, proliferation, and apoptosis of the melanoma cell line HTB-72. RT-PCR and IHC were performed to Investigate the possible mechanisms.

Results
The percentage of colonies of HTB-72 melanoma cells significantly decreased after treatment with jujube. This was correlated with the decrease in the optic density (OD) value of HTB72 cells after treatment with jujube. There were increased TUNEL+ cells and increased caspase-3 activity after treatment with jujube. These were associated with higher expression of anti-proliferative and pro-apoptotic expression of p21, p53, and TRAILR1.

Conclusion
Z. jujube inhibits HTB-72 melanoma cells via inhibition of proliferation and promotion of apoptosis by upregulation of p21, TRAILR1 and PCNA. Further investigation of jujube as a potential treatment for melanoma is warranted.

Senolytics improve neuromuscular function in a TDP-43 mouse model of amyotrophic lateral sclerosis

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Objective

Amyotrophic lateral sclerosis (ALS) is an incurable neurodegenerative disorder characterized by motor neuron loss, progressive loss of voluntary motor control, and eventual death. Accelerated biological aging, including DNA damage, inflammation, and mitochondrial dysfunction, exacerbates motor neuron degeneration in ALS. Sustained aging leads to cellular senescence, where cells lose the ability to undergo apoptosis and fail to adequately support motor neurons. We hypothesized that senolytics—drugs, such as dasatinib and quercetin, that induce apoptosis in senescent cells—could improve symptoms in a TDP-43Q331K ALS mouse model.

Methods

TDP-43Q331K mice were treated with senolytics dasatinib and quercetin (D+Q; 5 mg/kg and 50 mg/kg respectively) for six cycles (cycle=3 consecutive days every two weeks) starting at ~2.2 months of age. Motor behavior was assessed using rotarod and all-limb grip strength at baseline, 8 weeks and 15 weeks. Neuromuscular connectivity and excitability were evaluated at baseline and 15 weeks via compound muscle action potential (CMAP), motor unit number (MUNE), single motor unit potential, and cranial and cervical motor-evoked potentials (MEPs) as well as plantar flexion muscle contractility. mRNA levels of senescence markers (P21, P53, and BCL-2) were quantified terminally in harvested cortex, spinal cord, and gastrocnemius tissues.

Results

Compared to vehicle-treated TDP-43 mice, D+Q-treated mice showed: increased grip strength at 8 and 15 weeks and improved rotarod performance at 8 weeks, enhanced neuromuscular function, including higher CMAP, MUNE, plantar flexion muscle contractility, and cranial MEP at 15 weeks, and reduced mRNA expression of senescence markers (P21, P53, BCL-2) in the cortex, and P21 in the spinal cord and gastrocnemius.

Conclusion

D+Q treatment improves motor behavior and physiological measures of neural and neuromuscular function in ALS mice. These improvements are associated with a reduction in markers of cellular senescence. These findings highlight the potential of senolytics as a therapeutic approach for mitigating ALS symptoms.

Implementation of advanced molecular imaging to evaluate probiotic L. lactis bacterium capability to preferentially target orthotopic colorectal tumor

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Objective
To Implement advanced molecular imaging for real-time evaluation of the capability of probiotic facultative anaerobic bacterium Lactococcus lactis (L. lactis) to preferentially target orthotopic colorectal tumors.

Methods
Bioluminescent (BL) and fluorescent imaging were combined to simultaneously detect CRC tumors and L. lactis expressing infrared fluorescent protein (L. lactis-iRFP), respectively. To simultaneously detect BL and iRFP signals, we subcutaneously injected a CRC cell line expressing luciferase (CT26/luc) in the right flank of 6-week-old BALB/c mice. When tumors were palpable, L. lactis-iRFP was injected intratumorally.

Results
We found that BL and iRFP signals colocalized at the tumor site without directly overlapping without interfering one with another and L. lactis-iRFP signal was detected at the tumor site up to 5 days post-injection. Next, we proceeded to generate an orthotopic CRC mouse tumor model in 6-weeks-old BALB/c mice using the colonoscopy guided inoculation technique. We included two control mice without tumors, one administered with non-fluorescent L. lactis wild type, and the other with L. lactis-iRFP to compare the bacterium retention between tumor bearing mice. At day 11, when the orthotopic CRC tumor was well-established, the animals were administered with 1x1012 cfu/200 µL of L. lactis-iRFP or wild type via oral gavage, and BL and fluorescence signals were measured. The advanced molecular imaging revealed a strong iRFP signal in the tumor-bearing animals, up to 5 days post L. lactis-iRFP inoculation. The colons were scanned ex vivo and showed BL signal in the distal location of the CRC tumor. Interestingly, only the colons with tumors showed iRFP signal, suggesting that L. lactis-iRFP preferentially targets the CRC tumor microenvironment.

Conclusion
Additional experiments are required to reproduce this data and support a conclusion. We demonstrated that simultaneous detection of BL and iRFP signals is feasible and that this imaging technology could be potentially implemented for preclinical real-time evaluation of the capability of other bacteria to preferentially target solid tumors.

Exploring the therapeutic potential of H1-antihistamines in endometriosis: A gene regulation perspective

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Objective

Recent research underscores the role of immune dysregulation and inflammation in endometriosis (ES), a chronic condition affecting women's reproductive health and quality of life. While hormonal therapies are a standard, emerging treatments are exploring the possibility of targeting inflammatory pathways. Motivated by the literature that H1-antihistamines (H1-As) counter pro-inflammatory pathways that are also implicated in ES, in this work we assess the possibility of using H1-As within ES management through the lens of gene regulation.

Methods

We carry out differential gene expression (DGE) analysis on two high-throughput sequencing datasets of ES patients.

Results

Our findings highlight the dysregulation of several pro-inflammatory genes governing cytokine and chemokines, cellular adhesion, neuroangiogenesis, histamine synthesis and metabolism, and cellular apoptosis.

Conclusion

Building on our DGE analysis and a broader, ES-specific perspective on the role of granulocytes (e.g., mast cells) in histamine-mediated modulation of inflammatory cascades via the H1 histamine receptor (HRH1), we highlight compelling evidence supporting the potential therapeutic value of H1-antihistamines (H1-As) for ES. Active research into their anti-inflammatory, mast-cell stabilizing, and chemotherapeutic adjuvant properties further reinforces the need to explore H1-As as a treatment option.

Clinical management of atypical lobular hyperplasia of the breast

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Introduction

To evaluate the diagnostic approach, management, and outcomes of atypical lobular hyperplasia (ALH) in a postmenopausal woman presenting with breast masses, emphasizing personalized treatment strategies.

Methods

We reviewed the case of a 62-year-old postmenopausal female with a Tyer-Cuzick lifetime breast cancer risk of 6.7% and a recent right breast mass. Diagnostic imaging included bilateral mammography and targeted ultrasound. Imaging findings revealed heterogeneously dense breasts and two irregular masses in the left breast, classified as BIRADS 4C. Ultrasound-guided core biopsies were performed, revealing ALH concordant with imaging findings. The patient opted for surgical excision of both masses despite standard management guidelines recommending surveillance for concordant lesions.

Results

Pathological findings from the surgical excision confirmed atypical lobular hyperplasia without malignancy. The patient experienced an uneventful postoperative recovery. This case highlights the role of shared decision-making in managing ALH, particularly in patients with concordant imaging and pathology. While the standard of care for concordant ALH findings involves vigilant surveillance rather than surgical excision, this patient's decision highlights the importance of individualized care tailored to patient preferences and risk perception.

Conclusion

Effective management of atypical lobular hyperplasia relies on personalized diagnostics and treatment strategies. For concordant ALH, surveillance with regular mammography remains the standard approach. Surgical excision is reserved for discordant lesions, where imaging and biopsy findings do not align. Chemoprevention may be offered to reduce future cancer risk, particularly in high-risk patients. Clinicians should emphasize shared decision-making, balancing the risks and benefits of invasive procedures versus surveillance, to align treatment plans with patient preferences and clinical guidelines. Tailored care, early detection, and preventive strategies are critical to achieving optimal long-term outcomes in patients with ALH.

Advancing precision therapies for dravet syndrome with collaborative cross mouse models

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Objective

Dravet syndrome (DS) exhibits significant heterogeneity in clinical presentations and underlying pathophysiology, resulting in distinct disease subtypes. Individuals with SCN1A-associated DS often experience persistent seizures and progressive neurological impairments despite aggressive anticonvulsant therapy. This variability highlights the need for preclinical models that capture the broader spectrum of DS subtypes to enable the development of precision therapeutic approaches.

Methods

To address limitations in existing preclinical models, Collaborative Cross (CC) mouse strains were obtained from the UNC Systems Genetics Core Facility to introduce genetic diversity. Male 129.Scn1a+/– mice were bred with female CC mice to generate F1 progeny with null mutations, while wild-type controls (129.Scn1a+/+) served as comparators. Genotyping confirmed Scn1a and Gabra2 variants. Phenotypic assessments included hyperthermia-induced seizure assays, exploratory activity, motor coordination, and anxiety-like behaviors. Environmental factors such as temperature and humidity were monitored to evaluate their influence on seizure traits. Heritability analyses assessed the genetic background's impact on seizure threshold, duration, and severity. Data were analyzed using logistic regression, non-parametric tests, and clustering in R software.

Results

Two CC strains, CC011 and CC045, exhibited severe DS-like phenotypes characterized by heightened seizure susceptibility, frequent spontaneous seizures, and premature mortality, with approximately 50% of mice succumbing before study completion. Strain-specific variations in seizure susceptibility mirrored the clinical heterogeneity observed in DS patients. A B6J-specific Gabra2 variant further underscored the interplay between genetic, environmental, and sex-related factors in DS phenotypes.

Conclusion

These findings demonstrate that CC strains effectively model the genetic diversity and clinical variability of human DS. Their utility in identifying genetic modifiers supports the development of precision therapies tailored to specific DS subtypes, advancing translational research and therapeutic discovery.

Advancing inclusive healthcare: The role of LGBTQ+-centered training in medical education

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Objective
The prevalence of individuals identifying as LGBTQ+ is increasing, with some estimating that 28% of Gen Z falls within this community. Distressingly, many LGBTQ+ individuals experience anxiety seeking healthcare from fear of discrimination, mistreatment, or past medical trauma. The authors underscore the importance of curricula that educates rising providers on LGBTQ+ patient-centered care. This project aimed to assess attitudes and competency in LGBTQ+ care pre- and post-intervention across two cohorts in two consecutive years (2022-2023, 2023-2024).

Methods
Pre-series and post-series surveys assessed shifts regarding attitudes and competency in LGBTQ+ care. Questions were categorized as "clinical" (LGBTQ+ medical competency of participant) or "non-clinical" (personal beliefs regarding LGBTQ+ individuals). Permitted responses assessing agreeableness included "strongly disagree", "disagree", "agree", or "strongly agree" - to which a numerical value of 1-4, respectively, was assigned. Six questions with negative connotation were reverse-scored to mitigate response bias and ensure consistent measurement of concepts. Weighted measures were calculated to compare pre-series and post-series responses. Two-way ANOVA and post-hoc tests for both cohorts were run to determine significance.

Results
114 and 69 participants combined answered the pre-series and post-series survey, respectively, across both years. Both cohorts showed significant positive shifts both years regarding clinical questions (p-value = <0.001) and non-clinical questions in the second cohort. (p-value = 0.04).

Conclusion
Student-led, faculty-taught initiatives represent an important avenue by which clinical skills and personal perspectives regarding marginalized communities can be developed. Participants expressed confidence in their ability to care for, and understand issues impacting, LGBTQ+ patients. Additionally, statistically significant changes in answer agreeableness were largely driven by the clinical components of the educational series, and to a lesser extent the non-clinical aspects. Limitations included attrition and survey anonymity, which precluded tracking individual respondents.

Yittrium-90 radioembolization of unresectable hepatocellular carcinoma: A single center experience

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Introduction
Hepatocellular Carcinoma (HCC) is the most common malignant tumor and is often unresectable due to poor liver function from pre-existing cirrhosis. As a result, the prognosis of unresectable HCC is extremely poor. Therefore, the purpose of this study was to assess overall survival (OS) and identify adverse predictors of OS at 12 months after Y-90 radioembolization for unresectable HCC.

Methods
Retrospective review of patients that underwent Y-90 radioembolization for unresectable HCC from 2018 to 2021 was performed. Basic demographics, comorbidities, radiation dose to tumor, disease status at 3, 12 and 24 months, tumor distribution (unilobar vs bilobar), BCLC score, and laboratory data were gathered. Death during the follow up period or lost to follow up data was also recorded. The primary endpoint was OS at 3, 12, and 18 months. Intergroup comparisons were performed using unpaired t-test (Welch's t-test) or Pearson's Chi-squared test for predictors of OS at 12 months. Kaplan Meier was used to model OS following Y-90 radioembolization. Statistical significance was set at p value <0.05.

Results
In total, 48 patients that underwent Y90 mapping for unresectable HCC were screened, of which 4 patients (8.3%) passed away before undergoing Y90 radioembolization. As a result, 44 patients (39 Male, mean age 66.5 +/- 6.71 years) that underwent radioembolization were analyzed for this study. Technical success was achieved in 100% of cases. Thirteen patients (29.5%) underwent more than one Y90 radioembolization procedure. The OS rate was 91%, 70.5% and 43.2% at 3, 12, and 18 months, respectively (Fig 1). Univariate analysis identified hepatitis C infection (p =0.03), elevated pre procedural alpha-fetoprotein levels (p=0.02), and diabetes mellitus (p=0.03) adversely predicts OS at 12 months.

Conclusion
Y-90 radioembolization is a safe and can prolong the OS of patients with unresectable HCC. HCC secondary to hepatitis C, elevated alpha-fetoprotein, and diabetes mellitus adversely impacts OS at 12 months after Y-90 radioembolization.

Identifying changes in retinal dopamine signaling networks in age-related macular degeneration

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Introduction

The objective of this study was to identify changes in retinal dopamine signaling networks in age-related macular degeneration (AMD) by examining the expression of genes involved in the dopamine signaling cascade. Understanding these changes could shed light on the role of dopamine in retinal degeneration and its potential as a therapeutic target for AMD.

Methods

A list of 69 genes involved in dopamine signaling pathways was identified through a literature review and UniProt database query. Expression scores for these genes were obtained under baseline conditions (normal physiology) and compared to expression data from AMD cases. A log fold change analysis was performed, with genes exhibiting a log change greater than 1 in absolute value considered significantly altered in expression.

Results

Out of the 69 genes analyzed, 34 showed significant changes in expression between baseline and AMD conditions. Thirty genes exhibited increased expression in AMD, including genes involved in calcium signaling and protein phosphorylation. Four genes involved in calcium signaling, calcium homeostasis and glutamatergic neurotransmission showed decreased expression in AMD. These results suggest alterations in retinal dopamine signaling in AMD, with a predominance of genes showing increased expression.

Conclusion

This study identified specific genes involved in dopamine signaling that are differentially expressed in AMD, highlighting potential targets for further research into therapeutic strategies aimed at modulating dopamine receptor pathways. Understanding these changes could provide insights into the mechanisms underlying retinal degeneration in AMD and inform the development of future treatments.

Use of electromagnetic signaling for guided bone regeneration

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Introduction

Bone tissue engineering presents formidable challenges in achieving effective integration of implants with host tissues, particularly in the context of long bone defects. This investigation focuses on the potential application of using rectified electromagnetic field (REMF) to promote proliferation and directed migration of living cells for bone tissue regeneration. This research aims to develop non-invasive methods that enhance cellular activity and accelerate the healing trajectory in bone tissue engineering.

Methods

In this study, Helmholtz coils were employed to generate a directional, uniform REMF (0.5–2 milli Tesla, 15–100 Hz) to assess its impact on osteoblast behavior within a controlled culture system. We also evaluated the effect of REMF exposure time on osteoblast proliferation.

Results

The results showed that higher frequencies and magnetic strengths (e.g., 100 Hz, 2 mT) positively contribute to cell proliferation compared to lower strengths, while longer exposure time decreased the cell proliferation.

Conclusion

While higher REMF strengths and frequencies contribute to increased cell proliferation, effect of exposure time needs to be assessed to determine optimal parameters for osteoblast livability.

Molecular myelin dysfunction in the most common inherited peripheral neuropathies – CMT1A and HNPP

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Introduction

Increased and decreased dosage of the Peripheral Myelin Protein 22 (PMP22) gene cause dysmyelinating peripheral neuropathy, indicating that precise PMP22 expression is required for normal myelination. PMP22 duplication causes Charcot-Marie-Tooth Disease Type 1A (CMT1A) and PMP22 deletion causes Hereditary Neuropathy with Liability to Pressure Palsies (HNPP). CMT1A and HNPP are the most common inherited peripheral neuropathies, yet many gaps remain about their pathophysiology and pathomechanims. Our previous results with CMT1A model mice demonstrate that muscle atrophy occurs in the leg without evidence of secondary axon degeneration suggesting that primary myelin dysfunction may drive CMT1A pathogenesis.

Methods

We are using CMT1A and HNPP model mice and confocal immunofluorescence (IF) imaging of teased nerve fibers to determine how PMP22 underexpression and overexpression disrupts myelin integrity and identify CMT1A and HNPP pathomechanisms.

Results

PMP22 is a member of the Claudin superfamily so we first characterized adhesion junctions by IF in teased nerve fibers. We identified dramatically disorganized adherens junctions (AJs) at Schmidt-Lanterman incisure (SLI) transport channels in CMT1A and HNPP. AJ patterning at SLIs is more compact/punctate in CMT1A and more spread out in HNPP. The SLI components MAG and Connexin29 are also disorganized in CMT1A but appear more spread out with focal accumulations often outside of SLIs. Connexin29 also associates with Kv1 channels which led us to evaluate Node of Ranvier patterning. Kv1.2 at juxtaparanodes, Caspr at paranodes and Nav at nodes all demonstrate abnormal patterning. The MAG, Connexin29, Kv1.2, Nav and Caspr defects are more dramatic in CMT1A than HNPP which correlates with patient symptom severity.

Conclusion

We identified dramatic SLI and Nodes of Ranvier patterning defects that could impair myelin sheath function and contribute to CMT1A and HNPP pathogenesis. Ongoing studies are aimed at testing our working model that PMP22 regulates AJs which in turn controls myelin architecture and ultimately peripheral nerve function.

A self-calibrated, wearable vital sign monitoring device enabled by edge computing

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Introduction

Wearable technology is transforming healthcare by enabling personalized and proactive medical care. Continuous vital sign monitoring is essential for early disease detection and prevention, but many wearable solutions face challenges such as low signal quality and reliance on cloud connectivity, raising concerns over data security and latency.

Methods

This study introduces a wearable device equipped with four MAX30101 photoplethysmogram (PPG) sensors and an edge computer. The edge computer utilizes a pre-trained Bayesian optimization model for self-calibration, ensuring high-quality pulse waveforms for continuous monitoring of heart rate (HR), respiratory rate (RR), and blood pressure (BP). HR and RR are directly derived from PPG signals, while BP is predicted using pulse wave velocity (PWV) and predictors (age, gender, HR, weight, height) through a multilayer perceptron (MLP) model.

Results

The Bayesian optimization model achieved optimal calibration for 90% of the data, ensuring accurate pulse waveform quality. Testing on 20 participants (aged 17–49) across varying skin tones showed an average HR difference of 3.21 beats per minute (BPM) and ±1.55 breaths per minute (BrPM) for RR. Systolic and diastolic BP predictions achieved R^2 scores of 0.94 and 0.89, respectively.

Conclusion

The proposed device autonomously calibrates within 60 seconds, delivering accurate measurements of HR, RR, and BP. Significance: This device advances healthcare technology by enabling secure, real-time monitoring of vital signs, supporting early diagnosis, better cardiovascular health management, and enhanced well-being.

Specific transcription factors recapitulate cell identity of 10B neurons in the drosophila ventral nerve cord

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Introduction

During nervous system development, individual stem cells divide and give rise to a population of neurons called a lineage. There are 34 lineages in the ventral nerve cord (VNC) of Drosophila melanogaster (fruit fly), which is analogous to the vertebrate spinal cord. The adult nervous system is built during metamorphosis from neurons of these lineages. Leveraging genetic tools available in the fruit fly, I aim to investigate the molecular mechanisms driving the development of lineage 10B neurons within the adult nervous system.

Methods

Two recently published datasets have made the fly VNC a unique model system to study neural circuit development: single cell RNA sequencing (scRNAseq) provides transcriptome profiles for individual neuronal lineages and Electron Microscopy (EM) volume provides synaptic connectivity among neurons at a single synapse resolution. EM volume identified a group of proprioceptive sensory neurons, the femoral chordotonal (FeCo) neurons, that make strong synaptic connections with 10B neurons. scRNAseq analysis identified a set of key genes likely involved in cell-fate acquisition, axon guidance, and synapse formation of 10B neurons. Using this information, I will perform gain or loss of function experiments to elucidate which transcription factors are essential for 10B identity and which cell-to-cell communication molecules are needed for 10B neurons to integrate into neuronal circuits, particularly those with the FeCo neurons.

Results

Preliminary results indicate that the 10B lineage has approximately 72 neurons per neuromere. We have identified 3 distinct subsets of 10B neurons within the scRNAseq data set. We are currently working to identify essential transcription factors and key guidance molecules from the scRNAseq datasets.

Conclusion

Our research will lead to the understanding of molecular pathways underlying cell fate and lineage identity of 10B neurons and the circuits they form. Moving forward, we will manipulate components of this system to better understand circuit formation.

Developing a broad range in vitro system to probe for plant based translational inhibitory compounds

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Introduction

Determine if the E. Coli S30 Extract System can detect plant-based translational inhibitors from crude extracts.

Methods

Crude plant extracts were prepared using a chloroform and 25% ethanol extraction protocol with guidance from Dr. Craig Schenck. The E. Coli S30 Extract System for Circular DNA (Promega), containing S30 isolate (contains transcription/translation machinery), pre-mix, amino acids, and the pBESTluc DNA template (luminescent protein template), was used to test these extracts for inhibitory effects. Luminescence measurements were taken via plate reader after adding Luciferase Assay reagent. For sensitivity testing, omacetaxine mepesuccinate (from Cephalotaxus harringtonia) served as a positive control and standard curve. Crude extracts of Cephalotaxus harringtonia were tested at 1:22, 1:11, and 3:22 dilutions, with 25% ethanol controls.

Results

Pure omacetaxine mepesuccinate significantly reduced luminescent signal ($p<.001$) and exhibited linear inhibition between 40nM and 145nM. The crude extract of Cephalotaxus harringtonia also demonstrated significant translational inhibition ($p<.01$) in 1:23 and 2:23 dilutions, independent of ethanol presence.

Conclusion

These findings confirm that the E. Coli S30 Extract System can detect translational inhibitory compounds from plant crude extracts, validating the developed protocol. This protocol is now being extended to a wide range of plants, with potential applications for identifying antibiotic, antiviral, and anticancer compounds. Future work will include testing on Staph, human cell lines, and other pathogens using an in-house in vitro transcription/translation system.

Real-time movement data collection and agent-based model enhancements to understand antimicrobial resistance dynamics in healthcare settings

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Introduction

Asymptomatic carriers and contaminated medical devices are major contributors to the spread of antimicrobial-resistant (AMR) pathogens in healthcare settings. While Agent-Based Models (ABMs) have been widely used to explore host-pathogen-environment interactions, their predictive accuracy is often questioned due to the lack of real-world movement data. This study aims to enhance the accuracy of ABMs by incorporating real-time movement and contact data of healthcare workers and medical devices, with the goal of better understanding and mitigating the transmission dynamics of AMR pathogens in healthcare environments.

Methods

We utilized indoor GPS technology to collect real-time movement and contact data of healthcare workers and medical devices at University Health Truman Medical Center (UHTMC). This data was integrated with historical patient medical records and was fed into a series of candidate ABM to investigate how movement patterns can potentially impact on AMR transmission.

Results

By incorporating these real-time movement data into ABMs, we observed a substantial improvement in the predictive accuracy of the models. The model analysis revealed that the movement patterns of healthcare workers and medical devices play a significant role in influencing the spread of AMR pathogens within the hospital.

Conclusion

Integrating real-time movement and contact data into ABMs enhances their ability to predict AMR transmission dynamics in healthcare settings. This approach provides a more robust framework for understanding and mitigating the spread of antimicrobial resistance in hospitals.

Establishment of translational luciferase-based cancer models to evaluate antitumoral therapies

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Introduction

Orthotopic cancer models represent a valuable opportunity to better understand how cancer cells behave and produce tumors in their primary organs, as well as how the local microenvironment can affect the tumor development. Our aim was to produce cancer cell lines capable of emit light to follow the growth of tumors located at the interior of the body of live animals. This study focuses on the development of a platform to evaluate the efficacy of antitumoral therapies more accurately using a bioluminescent (BL) imaging system.

Methods

We developed luciferase-based cancer cell lines that can emit BL and when inoculated orthotopically, they produce solid tumors that can be detected in live animals, allowing for a more accurate model to evaluate antitumoral therapies.

Results

We stably transfected the triple negative breast cancer (TNBC) cell line from human origin HCC1937 with the luciferase expressing plasmid pGL4.50 [luc2/CMV/Hygro]. After transfection, the luciferase activity was tested in vitro and once confirmed these luciferase-expressing cell lines were inoculated orthotopically into synergic animals. We successfully established orthotopic BL tumors that could be detected by bioluminescence imaging, as well as the detection of distal metastases by this method. The signal from the tumors in vivo correlated with the signal detected from the ex vivo organs, confirming the high accuracy and sensitivity of the use of BL as a detection method for cancer models. Interestingly, we confirmed a change in the antiviral response after the plasmid internalization in the cell line HCC1937/luc2.

Conclusion

In our study, we offer a clinically relevant bioluminescent orthotopic cancer model that can be used to accurately evaluate the efficacy of antitumoral therapies by monitoring the tumoral growth and the appearance of metastases, with the advantage of allowing for multiple readings over time on live animals to assess the efficacy of antitumoral therapies.

Social determinants of health and their association with breast cancer versus other-cause mortality in U.S. women

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Objective

To examine and rank how multiple Social Determinants of Health (SDoH) factors affect breast cancer mortality compared to all other causes of death using a national population study dataset.

Methods

Leveraging the National Longitudinal Mortality Study (NLMS) dataset, we analyzed a cohort of 72,496 deceased women. Nine SDoH variables were selected based on completeness, collinearity, and clinical relevance, aligning with the Healthy People 2030 framework. Multivariable logistic regression assessed associations between SDoH factors and the odds of breast cancer mortality versus other causes of death. A random forest machine learning model ranked these factors by importance.

Results

Age was the most influential factor in determining whether a woman died from breast cancer versus other causes. When comparing breast cancer deaths to deaths from other causes: never married women (aOR=0.53, 95% CI: 0.45-0.62) and separated/widowed/divorced women (aOR=0.76, 95% CI: 0.69-0.84) had lower odds of dying from breast cancer compared to married women. Black women had lower odds of dying from breast cancer versus other causes compared to White women (aOR=0.73, 95% CI: 0.64-0.84). Women with college education had higher odds of dying from breast cancer versus other causes compared to those with high school education (aOR=1.46, 95% CI: 1.30-1.64). Health insurance type and household size also significantly influenced whether a woman died from breast cancer versus other causes.

Conclusion

Our findings support recent evidence showing higher breast cancer mortality among more educated women and reveal different patterns of cause-specific mortality between racial groups. The complex relationships between education, marital status, age, and race in determining mortality outcomes suggest the need for multifaceted, targeted interventions that consider multiple SDoH factors simultaneously.

The effects of nutritional or herbal supplement intake on lymphatic pain, daily living function, and emotional distress among breast cancer patients

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Introduction
The use of nutritional or herbal supplements (e.g., vitamins and antioxidants) are common among breast cancer patients. Patients take the supplements for various reasons, such as for pain on the affected body side or upper body after breast cancer treatment (i.e., lymphatic pain), better physical functions, better mood, or preventing cancer recurrence. This study aimed to investigate the effects of supplement intake on lymphatic pain, daily living function, emotional distress among breast cancer patients.

Methods
A cross-sectional study was conducted to enroll 567 breast cancer patients. Demographic, clinical data, and supplement intake information were collected. Lymphatic pain, daily living function, and emotional distress were measured using subscales in Breast Cancer and Lymphedema Symptom Experience Index. Multivariable logistic regression models were utilized to calculate the odds ratios (ORs) with 95% confidence intervals (CIs), quantifying the effects of various supplement intakes on lymphatic pain, daily living function, and emotional distress.

Results
The majority of the participants (83.43%) were taking supplements, only 16.57% never took any supplements. Older participants were more likely to take supplements ($t(129.52) = -3.32$, p-value < 0.001). The most common supplements taken were vitamins (77.77%), followed by calcium (34.92%), and minerals (14.28%). Less-commonly-used supplements included anti-inflammatory or antioxidant supplements (9.17%), cardiac health supplements (19.04%), probiotics (10.58%), supplements for skin and hair health (10.58%), and herbal supplements (12.52%). Subsequent multivariate logistic regression revealed that there were no significant associations between any supplement intake and lymphatic pain, daily living functions, or emotional distress.

Conclusion
Despite the wide use of supplements among breast cancer patients, no significant beneficial effects were observed regarding supplements on lymphatic pain, daily living functions, and emotional distress. These findings highlight the need for further research to discern the need for supplement intakes among breast cancer patients as some of supplements do have unintended and harmful effects.

Defining disparities – The impact of race and facility location on the length of stay of stereotactic implant patients

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Introduction

Stereotactic implantation can help reduce the motor symptoms of Parkinson's Disease, such as tremors and dyskinesia, in patients who have failed pharmacological treatment. The objective of this study is to address if race or hospital location has a greater impact on the length of stay (LOS) of these stereotactic implantation patients.

Methods

A retrospective analysis was performed of 1,040 stereotactic implantation patients from the Cerner Health Facts Database. We divided our patients into 4 groups based on race and hospital location: Urban White (1), Rural White (2), Urban Non-White (3), Rural Non-White (4). For each group, we calculated the median LOS and the interquartile range. Using the Dwass, Steel, Critchlow-Fligner Method (DSCF), we conducted pairwise comparisons between the groups.

Results

In the DSCF Test, there is a statistically significant difference between groups 1 and 2 ($p = 0.0047$) examining the impact of hospital location on LOS, and between groups 1 and 3 ($p = < 0.0001$) examining the impact of race on LOS. Because the p-value is smaller and DSCF-value is greater for the group 1 vs. 3 comparison, we can reasonably conclude that groups 1 and 3 are more dissimilar than groups 1 and 2. Because the group 1 vs 3 comparison examines the impact of race on LOS, this suggests that while both race and hospital location had a significant impact on length of stay, race had a greater effect.

Conclusion

Upon examining the literature, even after controlling for age, payer status, and income, studies have shown that Black patients were 5 times less likely to receive stereotactic implantation for PD than White patients, despite having characteristics warranting surgical treatment. This lack of neurologic treatment and decreased frequency of stereotactic implantation can explain why our data showed a significant difference in the outcomes of non-white patients.

Stable periodic solutions of a delayed reaction-diffusion model of Hes1-mRNA interactions

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Introduction

Hes1 (Hairy and Enhancer of Split 1) is a key gene involved in embryonic development and cellular differentiation. Its interaction with mRNA is crucial for regulating gene expression, influencing cell fate during development. Empirical studies have shown that Hes1-mRNA interactions exhibit sustained oscillations in specific cell types. However, existing mathematical models often fail to capture stable periodic solutions, limiting their explanatory power. Objective: This research aims to develop a mathematical model capable of accurately replicating the sustained oscillatory behavior observed in Hes1-mRNA interactions and to identify the conditions leading to these dynamics.

Methods

We propose a delayed reaction-diffusion model incorporating a time-delay parameter to represent the regulatory feedback in Hes1-mRNA interactions. Stability and bifurcation analyses are conducted to establish conditions for the emergence of delay-induced periodic solutions. Numerical simulations are performed to verify theoretical predictions.

Results

Our analysis identifies critical delay thresholds at which the system undergoes bifurcations, leading to stable periodic solutions. Numerical results confirm the theoretical findings, demonstrating the model's ability to replicate sustained oscillatory behavior.

Conclusion

The proposed delayed reaction-diffusion model successfully captures the stable periodic dynamics of Hes1-mRNA interactions observed in empirical studies. This work advances our understanding of gene regulation dynamics and provides a framework for studying similar oscillatory systems in developmental biology.

Temporal and spatial expression of regeneration-associated genes after spinal cord injury in zebrafish

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Introduction
Spinal cord injuries (SCI) in mammals often lead to permanent disability due to their limited regenerative capacity. In contrast, zebrafish recover full function following SCI. This study aims to investigate the temporal and spatial expression changes of pkd2l1, a marker gene for crucial cerebrospinal fluid-contacting neurons (CSF-cNs), during zebrafish spinal cord regeneration.

Methods
Single-cell RNA-sequencing was used to identify essential regeneration-associated clusters. Wild-type zebrafish underwent complete spinal cord transection injuries. At weekly intervals post-injury, spinal cords were cryosectioned and subjected to HCR in situ hybridization to visualize pkd2l1 expression. Confocal microscopy was used for imaging, and FIJI software quantified the number of pkd2l1-positive cells and their spatial distribution at defined regions rostral and caudal to the lesion site.

Results
Single-cell RNA-sequencing identified cerebrospinal fluid-contacting neurons (CSF-cNs) expressing pkd2l1 as regeneration-associated clusters, with pkd2l1 serving as a top marker for these neurons. pkd2l1 expression demonstrated significant temporal and spatial dynamics after spinal cord injury (SCI). Quantification revealed the highest pkd2l1 gene expression at 1 week post-injury (wpi; $p = 0.0067$) and the greatest number of pkd2l1-positive cells at 3 wpi ($p = 0.0257$). These changes were most pronounced at 450 µm rostral to the lesion site. Statistical analysis using two-way ANOVA confirmed the significance of these temporal variations, emphasizing the dynamic role of CSF-cNs in spinal cord regeneration.

Conclusion
The dynamic regulation of pkd2l1 in CSF-cNs post-SCI underscores their critical role in zebrafish spinal cord regeneration. This study provides foundational insights into the spatiotemporal dynamics of these neurons, advancing our understanding of vertebrate neural repair. Future work, a process currently underway, includes the development of transgenic zebrafish to ablate CSF-cNs, and aims to confirm their precise contributions to regeneration. These findings offer promising avenues for developing therapeutic strategies to address spinal cord injuries in humans.

5-HT2C agonism: A novel neurotherapeutic treatment for sarcopenia

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Introduction
Sarcopenia, the age-related loss of muscle mass and strength, leads to physical decline, frailty, and reduced healthspan. As the global population ages, the prevalence of sarcopenia is expected to increase. Effective treatments remain limited, with long-term strength training being the only proven approach, producing ~11% increase in strength assessments. Therefore, new strategies to improve physical function and strength in older adults are urgently needed. This study aims to investigate whether boosting motor neuron excitability could mitigate age-related declines in physical function and strength.

Methods
We used a selective 5-HT2C receptor agonist, believed to enhance motor neuron excitability by amplifying persistent inward currents. Aged mice were administered a single oral dose of lorcaserin (1.5, 3, or 6 mg/kg). Motor neuron excitability was assessed by measuring cervical motor evoked potential (cMEP) amplitude and cMEP attenuation during repetitive stimulation. Motor coordination was evaluated using rotarod performance, and functional strength was assessed through maximum weighted cart pull and grip strength tests. Additionally, we used a 5-HT2 receptor antagonist to test the effects of receptor blockade.

Results
A single dose of lorcaserin significantly increased motor neuron excitability and repetitive firing, evidenced by a 53-64% increase in cMEP amplitude and maintained repetitive cMEP amplitude. Lorcaserin also improved motor coordination, with a 22-24% increase in rotarod performance and enhanced functional strength (17% increase in maximum weighted cart pull and a 12% increase in grip strength). In contrast, blocking 5-HT2 receptors decreased cMEP amplitude by 26%, increased cMEP attenuation during repetitive stimulation, and reduced grip strength by 10%.

Conclusion
Our findings suggest that enhancing motor neuron excitability via the 5-HT2C receptor improves physical function and strength in aging. These results indicate that boosting motor neuron excitability could be a promising neurotherapeutic approach for treating sarcopenia and age-related physical decline.

Key predictors of in-hospital mortality and home discharge after stroke

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Introduction

Stroke is a leading cause of mortality and morbidity globally. Understanding in-hospital mortality and discharge destination provides valuable insights into patient prognosis and care planning. This retrospective cohort study evaluates predictors of in-hospital mortality and successful discharge to home or home health services in stroke patients using a comprehensive hospital data set.

Methods

Logistic regression models were used in a cohort of 374 stroke patients admitted to MU Hospital from 2011 to 2012 to assess predictors of "Expired" and "Home/Home Health Service" outcomes. Predictor variables included patient demographics, clinical characteristics, and treatment factors. Model performance was evaluated using the Akaike Information Criterion (AIC) and Area Under the Curve (AUC).

Results

Predictors of in-hospital mortality included higher illness severity (Wald $\chi^2 = 22.5618$, $p < 0.0001$) & (OR for extreme vs. minor severity: 28.182, 95% CI: 5.839–136.035, $p = 0.0001$), respiratory comorbidities (OR: 10.483, 95% CI: 3.56–30.87, $p < 0.0001$), and hemorrhagic stroke type (OR: 0.258, 95% CI: 0.079–0.835, $p = 0.0238$). The reduced model for predicting in-hospital mortality achieved an AIC of 179 and an AUC of 0.933, demonstrating strong predictive performance. Predictors of successful discharge included younger age (OR: 1.056 per year, 95% CI: 1.034–1.079, $p < 0.0001$), use of thrombolytic therapy (OR: 3.518, 95% CI: 1.195–10.355, $p = 0.0224$), and absence of neurological complications (OR for neurological vs 0: 3.069, 95% CI: 1.456–6.465, $p = 0.0032$).

Conclusion

This study identifies significant predictors of in-hospital mortality and successful discharge among stroke patients, highlighting the critical roles of illness severity, respiratory and neurological comorbidities, and treatment factors (thrombolytics, antiplatelets, anticonvulsants). These findings offer valuable insights for clinical risk stratification, discharge planning, and improved cost efficiency in stroke care.

In vivo advanced molecular imaging of the probiotic L. lactis expressing fluorescent proteins to monitor its transit through the gastrointestinal tract

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Introduction

To evaluate and characterize the use of advanced molecular imaging to monitoring L. lactis transit through GI tract and determine its feasibility as diagnostic tool or determine whether L. lactis targets preferentially the harsh hypoxic, and/or acidic microenvironment of digestive pathologies including, colitis, adenomatous polyps of the colon or colorectal cancer.

Methods

Recombinant strains of probiotic bacterium Lactococcus lactis expressing different fluorescent proteins were orally administered to C57BL/6 and Balb/c mice, their transit through the GI tract was monitored by in vivo advanced molecular imaging and multispectral optoacoustic tomography (MSOT) at different time points. The L. lactis-fluorescence intensity in live animals was quantified using the software Aura 4.0.7.

Results

We found that the green channel to detect L. lactis-GFP results in a strong tissue autofluorescence in both C57BL/6 and Balb/c mice and the signal from L. lactis-mCherry could not be detected in neither black nor withe mice because the red wavelength lacks enough deep tissue penetrance to pass through the intestines and the abdominal wall. In contrast, L. lactis-iRFP bacterium produce a strong, specific and well-localized signal, that was detected in real-time for up to 24 h after oral gavage administration in Balb/c (white) mice, whereas in C57BL6 (black) mice it could be detected with an unspecific signal which suggests that melanin excess may interfere with the detection of L. lactis-iRFP. The pilot MSOT imaging revealed that biliverdin, the iRFP substrate generated a strong signal which made it difficult to distinguish between the negative controls and L. lactis-iRFP, therefore additional optimization is needed.

Conclusion

These results suggest that L. lactis-iRFP in Balb/c is an excellent model to monitoring the bacterial presence, permanence and interactions with the anatomical structures while transiting through the GI tract. Additionally, optoacoustic tomography imaging requires further optimization and improvement.

Enhancing personalized treatment recommendations through federated survival analysis

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Introduction
To develop and evaluate a federated survival analysis framework that addresses data heterogeneity across medical centers, enhancing personalized treatment recommendations for cancer patients while preserving data privacy. The framework integrates state-of-the-art survival analysis models, both traditional and neural network-based, to provide comprehensive and accurate survival predictions.

Methods
The study employed a federated learning approach centered on the Cox Proportional Hazards (CoxPH) model and extended it to state-of-the-art neural network models for survival analysis, including DeepHit, Deep Survival Machines (DSM), Dynamic DeepHit, and the Random Survival Forest-based neural network (RSF-NN). These models were evaluated on both synthetic datasets and real-world data from the Surveillance, Epidemiology, and End Results (SEER) database. Feature-based clustering was implemented to manage data heterogeneity, and an event-based reporting strategy dynamically adapted the models to local data changes. This multi-model framework was designed to compare the performance of traditional and neural network-based approaches in federated learning settings.

Results
The federated framework demonstrated significant improvements in survival prediction accuracy and robustness across all models. CoxPH served as a strong baseline, while neural network-based models showed superior performance in capturing non-linear relationships and complex survival patterns. DeepHit and Dynamic DeepHit excelled in handling time-to-event predictions, while DSM and RSF-NN demonstrated enhanced performance in managing censored data and heterogeneous feature spaces. The integration of feature-based clustering and event-based reporting further optimized the performance of all models, achieving higher concordance index scores across diverse datasets.

Conclusion
This study highlights the potential of combining traditional survival analysis models with advanced neural network approaches in a federated learning framework. By addressing data heterogeneity, preserving privacy, and incorporating state-of-the-art survival analysis techniques, the framework advances the development of personalized treatment recommendation systems.

Mettl3 deficiency impairs mitochondrial function and indirect flight muscle development in Drosophila melanogaster

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Introduction
The purpose of our study was to uncover a conserved, muscle specific function for Mettl3 in indirect flight muscle (IFM) development in Drosophila melanogaster and to identify which molecular pathways are impacted by altered m6A RNA methylation.

Methods
mRNA Seq was performed on IFM tissue dissected from control, Mettl3 mutant, and muscle tissue specific rescue. We identified significantly misregulated genes in muscle lacking Mettl3 by performing a differential gene expression analysis using DESeq2. We used Gene Ontology, Gene Set Enrichment Analysis, and MitoXplorer to identify affected pathways and biological processes. Human disease association annotations were used to link differentially expressed genes to potential clinical relevance.

Results
Mettl3 deficient IFMs exhibited downregulation of numerous mitochondrial associated genes. Pathway analyses indicated that mitochondrial inner membrane components, ATP biosynthesis pathways, and transmembrane transport processes were significantly disrupted. Genes involved in mitochondrial fusion and tricarboxylic acid cycle function were notably reduced. Additional changes were observed in sarcomere proteins as well as synapses and neuronal development pathways. Confocal microscopy confirmed reduced Mito GFP expression in Mettl3 mutant IFM, suggesting impaired mitochondrial organization. IFM motor neurons lacking Mettl3 exhibit axon overbranching, implicating muscle and neuronal defects in flightlessness. Human gene annotations revealed overlap with muscular dystrophy gene sets, indicating potential translational relevance.

Conclusion
Loss of Mettl3 function in IFMs results in significant mitochondrial deficits, likely contributing to the flightless phenotype. The data support that m6A dependent regulation of mRNA stability and processing is essential for proper mitochondrial development and muscle function. Future work includes differential exon usage analysis via DEXSeq to understand alternative splicing changes, mapping m6A methylation sites to identify direct Mettl3 targets, and confocal imaging of mitochondria to visualize morphological disruptions. These approaches will deepen understanding of Mettl3 mediated m6A regulation in muscle development and may inform studies of related human disorders.

Discovering hit-to-lead compounds against Plasmodium falciparum polymerase

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Introduction

Antimalarial resistance is a worldwide threat causing 249 million infections and 608,000 deaths per year. Resistance is inevitable when using common malarial drugs such as chloroquine and artemisinin combination therapy (ACT). Both drugs target heme leading to cell death. The increased rate of resistance is due to many factors most of which fall into the categories: improper use of drugs, overuse of drugs, and poor living conditions. These factors have led to a rapid number of resistant populations.

Objective: Discover antimalarial drugs that can be effective against ACT resistant populations using novel targets. With no new compounds being discovered and ones in use becoming less effective infections are more deadly. With resistance developing so rapidly, novel drugs with novel mechanisms of action are in high demand.

Methods

A strategy in developing new drugs is to target a vital subunit of Plasmodium, which in this case is DNA polymerase. To inhibit the growth, replication, and maintenance of microbes the enzyme polymerase is an ideal enzyme to target. DNA polymerases generally have two common functions among all organisms, to replicate and repair the genome. Inhibition of the DNA polymerase will decrease the ability to divide and make the organism more susceptible to therapies that introduce double-stranded DNA breaks.

Results

We used purified malaria polymerase and computational docking to identify a novel binding pocket and in vitro assays guided by docking to assess the inhibitory effect of novel compounds. Conclusion: Multiple compounds showed inhibition of malaria polymerase at sub-micromolar concentration leading to promising outlook for future drug development.

Conclusion

Multiple compounds showed inhibition of malaria polymerase at sub-micromolar concentration leading to promising outlook for future drug development.

Latent autoimmune diabetes in adults: Diagnostic and management considerations in atypical diabetes presentation

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Introduction

Currently, criteria for LADA diagnosis consists of age >30 years, positive autoantibodies to islet β cells, and insulin independence for at least the initial 6 months after diagnosis. Patients with this condition often present with a lower BMI, an earlier age of diabetes onset (30-50 yrs) than classical DM2 (45-65 yrs), and a personal or family history of autoimmune disease. Our objective was to evaluate the efficiency of DM2 regimens on LADA patients and to suggest a broader diabetes diagnostic framework.

Methods

For this study, a case report analysis was completed, involving an 85-year-old female who presented with hyperglycemia and new signs of insulin dependence. This patient was previously diagnosed with DM2 but history and presentation were more consistent with LADA. Thorough analysis of disease progression, response to treatment, and LADA antibodies were completed to assess for a potential LADA diagnosis.

Results

The patient initially presented with hyperglycemic readings of >500 mg/dL persisting for three days, a lower BMI of 31.2, and poor response to oral hypoglycemic agents. Upon insulin administration, glucose levels stabilized but demonstrated concerns of hypersensitivity with morning hypoglycemia and rebound glucose with oral DM2 regimens. Diagnosis was confirmed with positive test results of elevated glutamic acid decarboxylase [GAD] autoantibodies at >250 IU/mL and islet antigen 2 [IA-2] autoantibodies at >350 U/mL.

Conclusion

Her initial diagnosis of DM2, development of insulin dependence at age 85, and later rectified diagnosis of LADA contributes to a growing body of literature surrounding the increasing prevalence of this condition. Elevated levels of pancreatic autoantibodies (i.e. GAD and IA-2) directly correlate with accelerated disease progression and increased risk of diabetic ketoacidosis. Thus, our case highlights the importance of challenging prior diagnoses of DM2 in patients with atypical diabetic presentation to improve management.

Caregiver inclusion influence on adolescent acceptance and engagement of an MHealth app, a RCT

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Introduction
As obesity rates continue to rise mobile health applications may play a role in reversing these trends by promoting health behavior change. Inclusion of adult caregivers haven't been well studied in adolescents. To address these knowledge gaps, we conducted a randomized controlled trial using the novel CommitFit mHealth app. We developed this app to engage adolescents and adult caregivers to set and achieve health behavior goals through gamification techniques. The purpose of this study is to evaluate three research aims: (1) determine whether adolescents find it acceptable to include caregivers in their mHealth lifestyle interventions, (2) evaluate whether caregiver engagement in mHealth lifestyle interventions is positively correlated with adolescent CommitFit mHealth app engagement based on their logging, and (3) explore whether including caregivers in adolescent mHealth lifestyle interventions increases the adolescent's self-perceived motivation to improve their health behavior.

Methods
In this 4-month RCT, 30 dyads (caregiver and adolescent) were randomized into three arms: CommitFit, CommitFit$ (adolescents received cash per point earned), and Waitlist Control. Dyad family team participation was encouraged. Adolescents completed surveys, and app utilization was evaluated with user-analytic software.

Results
Adolescents responded favorably to including their caregiver, with an overall score of 71.9 out of 100 that did not vary between groups. Caregiver app engagement was shown to be positively correlated with adolescent app engagement ($r=0.65$, $p = 0.002$). Pleasing caregivers was not a strong motivator for healthy behavior change (0.62 out of 3.00) in adolescents. However, there was a significant difference at 120 days between the CommitFit study arm and the control group (1.10 vs 0.20) ($p = 0.01$).

Conclusion
Adolescents may be willing to use mHealth apps that partners with their caregivers. While caregiver engagement may increase adolescent app use, adolescents do not perceive it to be an important motivator for health behavior change.

Remote breathing monitoring using LiDAR technology

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Introduction

This study aims to explore the feasibility of LiDAR technology for remote breathing monitoring by assessing its ability to measure respiratory metrics such as inhalation/exhalation patterns, respiratory rate, breath depth, and breath-holding episodes. The research emphasizes privacy-preserving and non-invasive approaches in diverse real-world settings.

Methods

Experiments were conducted using a Velodyne PUCK LiDAR sensor across five scenarios involving different subject orientations (front-facing, rear-facing, side-facing, and supine). Data processing included filtering point clouds for torso-specific regions, smoothing using a moving average filter, and detecting breathing metrics. The accuracy of breathing detection and the root mean square error (RMSE) for breath depth and respiratory rate were evaluated against manual ground truth data.

Results

The study demonstrated that LiDAR accurately tracks breathing patterns with varying success depending on sensor placement. Front-facing and supine scenarios showed the highest accuracy (1.00), while rear-facing orientation had the lowest performance (accuracy 0.73). Breath depth was measured with low RMSE values (0.0014–0.0020), and respiratory rate RMSE ranged from 0.00 to 3.21. The method effectively detected breath-holding episodes through moving variance analysis, highlighting the robustness of LiDAR in real-time respiratory monitoring.

Conclusion

LiDAR technology proves to be a promising tool for remote and privacy-preserving respiratory monitoring, overcoming limitations of traditional methods like invasiveness and environmental dependencies. Although sensor placement affects accuracy, the versatility of LiDAR across multiple scenarios demonstrates its potential for clinical and everyday health applications.

Clinic and histopathologic features of spitz nevi: A case series

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Introduction

Spitz nevi are rare, benign tumors in children that can resemble melanoma clinically and histologically. Congenital spitz nevi are symmetric, dome-shaped papules that grow rapidly for 6 months before stabilizing. Malignant transformation is rare; excision is recommended, as shown in 5 pediatric cases diagnosed as benign spitz nevi.

Methods

Retrospective chart review of patients was performed by searching ICD codes for that of “melanocytic nevi” and “malignant neoplasms of the skin” at University of Missouri between 9/1/2022 and 5/1/2024.

Results

5 cases of spitz nevi with differing characteristics.

Conclusion

Spitz nevi are rare, with limited published data on their epidemiology and distinguishing clinical features. The presented findings underscore the importance of clinical and histologic correlation in differentiating between benign and malignant atypical pigmented lesions in children.

Impact Statement

Spitz nevi are rare, benign melanocytic lesions that often mimic melanoma due to their clinical and histologic similarities, presenting a challenge in diagnosis, especially in children. While malignant transformation is rare, atypical variants may present with concerning features such as rapid growth, color changes, and size increase, necessitating careful evaluation. This study highlights the importance of histologic examination to confirm diagnosis and underscores the need for excision of suspicious lesions, as no definitive criteria currently exist to predict the biological behavior of atypical spitz nevi.

Establishing the natural history of synaptotagmin 1-associated neurodevelopmental disorder

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Introduction
Synaptotagmin 1-associated neurodevelopmental disorder (SYT1-NDD) is a rare and severe condition caused by mutations in the SYT1 gene, which encodes a key calcium sensor for synaptic vesicle exocytosis. The disorder manifests as cognitive impairment, motor delays, and psychiatric symptoms such as attentional deficits, emotional dysregulation, anxiety, and aggression. Although the molecular role of SYT1 in synaptic signaling is well-established, the clinical trajectory and variability of SYT1-NDD remain poorly understood. This study aims to address these gaps by tracking individuals with pathogenic SYT1 mutations and identifying biomarkers that may guide future therapeutic approaches.

Methods
This prospective natural history study will longitudinally assess cognitive, motor, and psychiatric symptoms in individuals with SYT1-NDD. Clinical, behavioral, and biomarker data—including neuroimaging and electrophysiological measures—will be collected to identify relevant central nervous system biomarkers that could aid in understanding disease progression. The study integrates both established and exploratory clinical measures, which will be adapted to developmental stages, ensuring that evaluations are age-appropriate and inclusive. Collaboration with patient advocacy organizations will shape data collection and interpretation, ensuring a patient-centered framework that aligns with the needs and priorities of affected families.

Results
The study aims to create a comprehensive natural history of SYT1-NDD, delineating key periods of disease progression and identifying potential therapeutic windows. Biomarker analysis is expected to offer new insights into CNS dysfunction, potentially informing the design of future clinical trials focused on gene-based and synapse-directed therapies. This research will provide critical data to improve the clinical management of SYT1-NDD and support the development of targeted therapeutic strategies.

Conclusion
By establishing a robust natural history of SYT1-NDD, this study will lay the foundation for transformative therapeutic strategies. It will also contribute to broader understanding of synaptic dysfunction in neurodevelopmental and psychiatric disorders, ultimately aiming to improve outcomes and quality of

A novel role of rostromedial tegmental nucleus in mediating the effects of fentanyl on sleep-wakefulness

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Introduction

Fentanyl is an analgesic and addictive substance which contribute to opioid use disorders (OUD), a chronic brain disease characterized by compulsive opioid use and harmful consequences. Although the critical association between fentanyl addiction and insomnia/sleep disruptions is known, the precise mechanisms through which fentanyl affects sleep-wakefulness has not been investigated. GABAergic rostromedial tegmental nucleus (RMTg), also referred to as GABA brake for midbrain dopaminergic systems, is a key structure in the μ-opioid receptor-dependent regulation of dopamine neurons. While this brain region is known to be a strong sleep promoter and projects to major wake-promoting centers including dorsal raphe nucleus, its role in fentanyl-induced sleep disruptions has never been examined. Thus, we propose that chemogenetic activation of RMTg will attenuate the wake-promoting effects of fentanyl.

Methods

To test this hypothesis, male C57BL/6J mice were infused with excitatory Designer Receptor Exclusively Activated by Designer Drug (DREADD; Gq), bilaterally in the RMTg (anteroposterior = –3.8 mm, mediolateral = 0.5 mm, and dorsoventral = 4.0 mm), along with implantation of sleep recording electrodes. The first set of experiments examined the effect of RMTg activation on spontaneous S-W during the dark period. The second set of experiments were designed to evaluate the effect of chemogenetic activation of RMTg on the wake-promoting effects of fentanyl (1.2 mg/kg, i.p.).

Results

Initial results suggest that mice administered with fentanyl (1.2 mg/kg, i.p.) significantly suppressed both NREM and REM sleep while promoting euphoria-like symptoms and long lasting insomnia. Chemogenetic activation of RMTg significantly mitigated the effects of fentanyl on the sleep-wakefulness.

Conclusion

Chemogenetic activation of the RMTg not only mitigates fentanyl's wake-promoting effects but also highlights its potential as a therapeutic target for addressing sleep disturbances associated with OUD. These findings provide new insights into the neurobiological mechanisms underlying opioid-induced sleep disruptions.

The effects of demographic variables on length of stay in stereotactic implantation

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Introduction

Our study aims to fill the gaps of past research by indicating which demographic factors are the most associated with increased LOS, while focusing on all stereotactic implants rather than specific conditions

Methods

A retrospective analysis was conducted on 179 acute status patients who underwent stereotactic implantation. Data was extracted from the Cerner HealthFacts database using CPT4 codes and a HCPCS code, then cleaned with R software. Bivariate association tests were implemented, including Wilcoxon Rank Sum test for dichotomous variables, Kruskal-Wallis test for socioeconomic status, and Pearson Correlation Coefficients for age and BMI. Payer status was categorized into government, other government, private, unknown, and worker's compensation groups.

Results

Gender significantly influenced LOS, with males having a higher median LOS of 25.0 hours compared to females at 6.0 hours ($p < 0.0001$). Contrary to the hypothesis, age showed a slight negative correlation with LOS (rho = -0.268, $p = 0.0003$). Tobacco users trended towards increased LOS compared to non-users, but this difference was not statistically significant ($p = 0.089$). Socioeconomic status, represented by payer groups, showed significant differences in LOS distribution ($p < 0.0001$), with the unknown payer group having significantly longer LOS compared to government, other government, and private groups. BMI showed no significant correlation with LOS ($p = 0.406$). Gender and age emerged as significant factors associated with LOS following stereotactic implantation, with males and younger patients experiencing longer stays. Socioeconomic status also played a role, though interpretation is limited by the unknown payer group. Tobacco use showed a trend towards increased LOS, while BMI had no significant impact. These findings provide insights for patient care and resource allocation in stereotactic implantation procedures, highlighting the need for further investigation into gender disparities and age-related factors affecting LOS.

Unraveling the mechanisms of Baker-Gordon Syndrome: A patient-derived model for precision medicine

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Introduction

At the synapse, neurotransmitter release is triggered by Ca2+-induced synaptic vesicle exocytosis, a process mediated in part by synaptotagmins (Syt). Heterozygous missense mutations in Syt1, the predominant synaptic protein in the central nervous system, has been linked to a rare neurodevelopmental disorder known as Baker-Gordon syndrome (BAGOS). It is broadly characterized by intellectual disability, developmental delays, seizures, and movement abnormalities. However, the severity and manifestation of these phenotypes are heterogeneous among affected individuals, with no evidence for a genotype-phenotype correlation. Furthermore, the pathogenic mechanisms associated with Syt1 mutations remain poorly understood, impeding therapeutic advancements. This underscores the critical need for precision medicine approaches that are tailored to the unique genetic profiles of patients, enhancing the potential success for treatment strategies.

Methods

To explore the underlying mechanisms of BAGOS and to develop targeted therapies, we used skin biopsies from BAGOS patients and their unaffected parent as controls. From these biopsies, we established fibroblast cultures that are differentiated through direct conversion into neuron-like cells or reprogrammed into induced pluripotent stem cells (iPSCs) to generate a broad range of neuronal subtypes.

Results

Using this innovative approach, we have generated patient-derived neurons, which exhibited altered morphological characteristics compared to aged-match and parent controls. Furthermore, future molecular analyses are planned to identify specific calcium-linked signaling pathways that are dysregulated in association with distinct Syt1 mutations. Combined, we have developed a patient specific human model of BAGOS that investigation of the impact of specific Syt1 mutations, specifically aimed at addressing the unique challenge of the heterogeneity inherent in BAGOS. These findings both enhance our understanding of the molecular underpinnings of BAGOS and pave the way for the development of precision medicine interventions that can be customized according to the distinct genetic variations present in each patient.

Development and testing of a precision siRNA therapy for SYT1 human variant mutations

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Introduction

Baker-Gordon syndrome (BAGOS) is a neurodevelopmental disorder caused by mutations in the SYT1 gene which codes for the protein synaptotagmin-1 (SYT1). SYT1 is a synaptic vesicle protein that couples action potentials with the synchronous exocytosis of neurotransmitters regulated by calcium binding to the C2A and C2B calcium-binding domains. Individuals with heterozygous missense mutations in the C2A or C2B domains present with hypotonia, developmental delay, intellectual disability, and emotional-behavioral disturbances. There are no known treatments or cures for Baker-Gordon syndrome. The majority of disease-causing human SYT1 variants have been shown to result in a toxic dominant-negative phenotype in cells. Autosomal dominant-negative disorders present with unique challenges, as therapeutics must distinguish between healthy and diseased alleles while maintaining high efficiency, specificity, and safety.

Methods

Our group has optimized an RNA interference (RNAi) approach to target a patient-specific SYT1-D366E mRNA sequence while demonstrating little to no interaction to wildtype SYT1 mRNA sequence. Small interfering RNAs (siRNAs) were systematically designed to span the D366E sequence region. These siRNA were then tested using an in vitro dual-luciferase system in a human cell line and promising siRNA candidates underwent further dose curve analysis.

Results

Our data demonstrates the ability for designing siRNAs to maintain high efficiency and specificity for targeting a dominant disease-causing allele that differs from the corresponding wildtype allele by a single base pair. To further test this allele-specific siRNA system in vivo, we have developed a mouse model harboring the relevant human DNA sequence and corresponding SYT1-D366E mutation.

Conclusion

We have provided evidence for the feasibility of using RNAi as a therapeutic intervention in BAGOS patients. After characterizing and testing our system in the engineered mouse model we will be able to further assess efficacy and safety of the approach setting the foundation for future preclinical trial studies.

The new UMKC Proteomics Core Facility

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Introduction

Showcasing of capabilities and services available at the new UMKC Proteomics Core Facility to the greater KC research community including quality control data that show the reproducibility of sample processing with the new LC/MS system.

Methods

The UMKC Proteomics Core is an NIH-supported facility housed in the UMKC School of Medicine. The facility includes a newly installed Orbitrap Eclipse Tribrid mass spectrometer and a Vanquish Neo UHPLC (ThermoFisher). To demonstrate the capabilities of this system we analyzed murine primary cell cultures generated from the optic nerve or retina, cultured human glial and neuronal cells, as well as commercially available cell lysate control samples. Each sample was processed multiple times using a Data Independent Acquisition (DIA) or a Data Dependent Acquisition (DDA) method with label-free-quantification and then analyzed via Spectronaut (Biognosys) or Proteome Discoverer (ThermoFisher). Spectronaut is the "gold standard" in DIA data analysis. Powered by its unique Pulsar search engine it produces the highest number of identifications and quantitative accuracy compared to other available software. For non-DIA analysis Proteome Discoverer, with its newly updated Chimerys search, excels at parsing samples containing proteins from multiple species. Both software packages are capable of advanced analysis methods including Post-Translational-Modification (PTM) localization, PTM quantification, and single cell proteomics analysis.

Results

Initial results showed excellent sensitivity and reproducibility: The average number of unique protein groups identified in the experimental group was greater than 8,000 and the coefficient of variation among technical replicates was less than 1%. Label-free-quantification results also showed an average coefficient of variation of less than 1% between technical replicates.

Conclusion

Our results show that our system and standard procedures are able to produce high-quality, reliable data. This is evidenced by our small coefficients of variation between technical replicates in both number of proteins identified and the quantification values of protein groups

Prevalence and epidemiological analysis of health conditions among south asian populations in Kansas City: Implications for culturally tailored healthcare strategies

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Objective

The South Asian community in the United States faces a disproportionate burden of chronic health conditions, including Type 2 Diabetes Mellitus (T2DM), cardiovascular disease (CVD), hypertension (HTN), and dyslipidemia (HLD). In Kansas City, where South Asians comprise 8.7% of the population, T2DM prevalence is up to four times higher than in White Americans, often occurring at lower body mass index (BMI) levels due to central adiposity and insulin resistance. Culturally tailored healthcare interventions have proven effective in improving outcomes, such as A1C levels, while enhancing patient engagement and satisfaction. This underscores the need to understand the specific health challenges within the Kansas City South Asian community to better address disparities.

Methods

A retrospective chart review was conducted using data from South Asian cultural clinics in Kansas City. Variables included age, gender, and birthplace (USA vs. foreign-born). Health conditions such as HTN, T2DM, HLD, and mental health concerns were analyzed.

Results

The study revealed that 38% of all patients had HTN, increasing to 59% among those over 50 years. T2DM was present in 39%, and HLD was observed in 48%. Men showed higher prevalence rates for HTN, T2DM, and HLD compared to women ($p<0.05$). Mental health analysis showed that 25% of patients scored >2 on the PHQ-9 scale, with 80% of these cases occurring in individuals under 35. There were no significant differences in prevalence between U.S.-born and foreign-born patients.

Conclusion

South Asians in Kansas City exhibit disproportionately high rates of HTN, T2DM, and HLD compared to other ethnic groups. The data emphasizes the importance of culturally informed prevention and treatment strategies. Future research should explore underlying factors driving these disparities to develop more targeted healthcare interventions.

Impact of repeated prenatal exposure to dexamethasone and ciclesonide on the developing brain of premature infants

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Introduction

Preterm birth poses significant challenges to neonatal health and necessitates the use of synthetic glucocorticoids (sGCs) to mitigate complications such as respiratory distress syndrome. Traditionally, betamethasone (BETA) and dexamethasone (DEX) has been the drug of choice to treat these complications where BETA is used commonly in the United States and both are used interchangeably in developing countries. While the administration of sGCs has proven effective in reducing complications associated with premature birth, concerns have emerged regarding its potential neurodevelopmental consequences like reduced brain size of the neonate and increased risk for psychological disorders such as depression and anxiety later on in the child's life. Ciclesonide (CIC), a pro-drug of inhaled corticosteroids, offers a promising alternative with fewer reported neurological disturbances. This study aims to investigate and compare the neurodevelopmental impact of prenatal exposure to sGCs compared with CIC in mouse models.

Methods

Pregnant mice were subjected to repeated doses of CIC, DEX, or vehicle at embryological day 14 and 16, and postnatal assessments were conducted. Histological brains were examined for markers of (1) proliferation including Ki67, Sox2, Tbr2, and Phosphohistone H3; (2) mature neurons including CTip2 and Beta tubulin; (3) oligodendrocytes, glial cells, and myelination with CNPase, Olig2, GFAP; (4) inflammation with Ib1a. Brain weight and depth of the cortex was measured and compared between groups.

Results

Studies are in progress to examine the long-term consequences of these drugs on rodent behavior. Our preliminary findings underscore the importance of exploring the molecular pathways underlying sGC exposure and its neurological consequences, paving the way for informed therapeutic strategies and improved neonatal care practices.

Conclusion

Ultimately, the identification of CIC's brain-sparing properties holds promise for protecting the long-term neurological health of premature infants.

Comparative effectiveness of MIGS stents in reducing IOP: A retrospective analysis

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Introduction

Glaucoma, the second leading cause of irreversible blindness worldwide, is primarily managed by reducing intraocular pressure (IOP), the main modifiable risk factor. Minimally invasive glaucoma surgery (MIGS) using stents has emerged as a preferred alternative to trabeculectomy due to a more favorable safety profile and faster recovery. However, limited data exists comparing the efficacy of various MIGS stents. This study evaluates and compares the effectiveness of six MIGS stents in reducing IOP over time.

Methods

A retrospective analysis was conducted on 226 MIGS procedures performed at Jones Eye Center in West Plains, Missouri, between November 2017 and July 2024. The stents analyzed included Hydrus (n=11), iStent (n=55), OMNIHydrus (n=18), OMNIiStent (n=77), OMNIVisco (n=17), and Xen (n=48). Preoperative IOP and IOP measurements at 3, 6, 9, and 12 months post-procedure were collected. Outliers were excluded, and percentage reductions in IOP were calculated relative to baseline. Statistical analysis was conducted using Mixed-Model ANOVA and Bonferroni tests for pairwise comparisons.

Results

Xen demonstrated superior IOP reduction compared to OMNIiStent at 3 and 6 months ($p = 0.0033, 0.0006$) and outperformed iStent at 6, 9, and 12 months ($p = 0.0142, 0.0373, 0.0043$). No significant differences were observed between Xen and other stents, nor among the other stents themselves. Xen's enhanced performance may reflect its use in patients with higher baseline IOP.

Conclusion

Xen achieved greater IOP reduction than OMNIiStent and iStent in both short- and long-term follow-up. These findings suggest that Xen may be particularly advantageous for patients with severe glaucoma or elevated baseline IOP. Further research with a larger population would be necessary to confirm these results and optimize MIGS stent selection for individual patients.

Mechanical performance of active implants made from near-infrared light response shape memory polymer composites

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Introduction

Near infrared light can potentially stimulate deeply implanted shape memory medical devices due to the capability of long wavelength light to penetrate tissues. The objective of this research was to determine the mechanical capabilities of light responsive polymers and their potential to shape change with the purpose of performing certain therapeutically indicated applications such as membrane puncture, bending metallic substrates, and moving soft tissues.

Methods

Near-infrared (NIR) light-responsive shape memory polymer composites (LSMPC) were produced from the polymers polycaprolactone (PCL), gelatin metacryloyl (GelMA), and polylactide-co-glyocolide (PLGA) mixed NIR light responsive graphene or iron oxide nanoparticles. Deformed from their memorized shape, the composites were exposed to NIR light in different distances with or without obstructive tissue in a small animal cadaver model between light source and material.

Results

The GelMa with graphene nanoparticles LSMPC were able to restore their memorized shape after up to 15 minutes NIR light exposure in up to 30 mm distance and 20 mm tissue thickness between light source and implant. Experiments are ongoing for the other LSMPC to determine whether they can puncture a membrane and bend magnesium sheets.

Conclusion

GelMA/graphene NIR light-responsive LSMPC have proven feasibility to be activated and change shape even in deeper tissue locations despite surrounding tissue obstructing the shape change. This capability depends on the type of polymer, the concentration of nanoparticles, and the light energy density. This system bears great potential for NIR light-controlled shape change implants to simplify select surgical procedures.

Low circulating FGF-21 after high protein intake likely mediates the adverse effect of high protein intake on endothelial function

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Objective

Endothelial dysfunction is an early marker of cardiovascular disease (CVD). A Western-type diet is a major risk factor for CVD, presumably because of the high intakes of simple sugars and red and processed meats with high salt, saturated fat, and cholesterol contents. Results from studies in animal models and population studies suggest high protein intake also contributes to CVD burden, but the mechanisms involved are unclear. Here we tested the hypothesis that high protein intake adversely affects endothelial vasodilator function, and this effect is at least in part mediated by the inhibitory effect of high protein intake on FGF21 production.

Methods

First, we evaluated the effect of a high-protein (HP) mixed meal (23% of energy as protein), compared with a standard protein (SP) mixed meal (15% of energy as protein), on plasma FGF21 concentration and reactive hyperemia, an established marker of endothelial function, in eighteen middle-aged (49 ± 14 years) participants with overweight/obesity (body mass index: 28 ± 3 kg/m2). Secondly, we evaluated the effect of escalating doses (0-50 ng/ml) of FGF21 on endothelial nitric oxide synthase (eNOS) phosphorylation at Ser1177 (stimulatory) and Thr495 (inhibitory) and nitric oxide (NO) production in cultured human umbilical endothelial cells (HUVEC).

Results

Plasma FGF21 concentration was significantly lower (by 65.0 ± 8.4 %, mean ± SEM) after the HP compared with the SP meal. The reactive hyperemia index was unchanged from basal conditions after the SP meal and decreased by 21 ± 3 % after the HP meal. Recombinant human FGF-21 treatment of HUVECs significantly decreased p-Thr495 eNOS and increased p-Ser1177 eNOS and NO production in a dose-dependent manner.

Conclusion

High-protein meal consumption impairs endothelial function, at least in part by lowering circulating FGF-21. These findings provide a potential mechanism for the increased CVD risks associated with high protein intake.

Catatonia and Health Disparities: The Impact of Insurance Status on Length of Stay In Hospital

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Introduction
To investigate how insurance status correlates with the length of hospital stay (LOS) among patients diagnosed with catatonia. The study aims to address healthcare disparities by exploring the intersection of socioeconomic factors and clinical outcomes.

Methods
A retrospective analysis of electronic medical records from hospitals using Cerner was conducted. Patients with catatonia were categorized into three groups based on insurance status: government-funded (e.g., Medicare, Medicaid), private insurance, and uninsured. Individuals with missing or invalid insurance information and extreme LOS exceeding 300 days were excluded. The Kruskal-Wallis test was used to assess LOS differences among groups, with Dunn's post-hoc analysis for pairwise comparisons.

Results
Among the 833 patients included, the median LOS varied significantly by insurance type: government-funded (8 days), private (9 days), and uninsured (3 days). The mean LOS was highest for government-funded patients (13.7 days) and lowest for uninsured patients (5.5 days). Statistically significant differences were observed between uninsured patients and those with government-funded ($p=0.0001$) or private insurance ($p=0.0003$). However, no significant difference was noted between government-funded and private insurance groups ($p=1.0$). These findings suggest financial barriers may contribute to shorter LOS among uninsured patients, potentially leading to poorer outcomes and higher readmission rates.

Conclusion
Insurance status significantly impacts LOS for patients with catatonia, with uninsured patients experiencing shorter hospital stays than those with government-funded or private insurance. This may reflect financial pressures leading to early discharge among uninsured patients, compromising care quality and increasing health risks. Addressing these disparities is critical for ensuring equitable treatment and improving healthcare outcomes. Future research should explore factors such as resource allocation, discharge planning, and access to follow-up care to mitigate systemic inequities in healthcare delivery.

Antimicrobial resistance in abdominal trauma-related infections

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Objective
Interest in antimicrobial resistance (AMR) has increased over the last few years due to its increasing prevalence and threat to public health. AMR refers to a pathogen's ability to develop resistance against classic antimicrobials previously known for their effectiveness. AMR caused the death of 118,000 people suffering from abdominal trauma-related infections in 2019. Although there are targeted antibiotics for such bacteria, as time has evolved, many of these infections have developed resistance to such treatments and thus caused much more severe infectious processes. It is important to understand the field itself and future developments that can be made to decrease the incidence of AMR infections.

Methods
We conducted a comprehensive literature review using PubMed. The search was limited to English-language articles and included the terms antimicrobial resistance, AMR, abdominal trauma and AMR, and similar terms. Additional relevant studies were identified by manually reviewing the reference lists of the selected articles.

Results
Antibiotic resistance can be developed through mutations, acquisition of resistance genes, conjugation, or efflux pumps. ESKAPE —an acronym representing the most common and concerning bacteria responsible for multidrug-resistant infections pose significant challenges as they exhibit resistance to various classes of antibiotics. In addition to modifying antimicrobial regimens, surgical interventions may also play a critical role in managing such infections. Other techniques for fighting such infections have been developed such as the use of nanotechnology, personalized medicine, and more.

Conclusion
Many discoveries have been made in the field of AMR, particularly in the case of abdominal infections caused by trauma. Although antibiotics are the mainstay treatment, this field needs to be understood more thoroughly to avoid increasing antibiotic resistance with such pervasive infections and come up with additional treatment methods.

Neural responses to fear-relevant stimuli: Early and sustained attention to snakes and angry faces

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Introduction
Studies have shown that threatening stimuli, such as snakes, spiders, and angry faces, elicit an Early Posterior Negativity (EPN) in the event-related potential compared to neutral stimuli, highlighting the evolutionary advantage of rapidly detecting threats. This study investigates whether snakes and angry faces elicit differential EPN as well as Late Positive Potential (LPP) responses. In doing so this study explores early visual attention (150-300 ms post-stimulus onset) and sustained motivated attention (300–500 ms post-stimulus onset).

Methods
Thirty-two participants (M = 21.1 years, 16 men, 16 women) viewed images of snakes, lizards, angry faces, and neutral faces in a rapid serial visual presentation (RSVP) task while their electroencephalogram (EEG) was recorded. The EPN was analyzed in 150–225 ms and 225–300 ms time windows, and the LPP was examined in the 300-500 ms window. Fear of snakes was measured using Snake Anxiety Questionnaire (SNAQ). Emotional valence and arousal ratings were also collected after the task.

Results
Threatening stimuli (snakes, angry faces) were rated as more unpleasant and arousing than non-threatening stimuli (lizards, neutral faces). Between 150–225 ms and 225–300 ms, there was a larger EPN for snakes (vs. lizards) than for angry faces (vs. neutral faces). The LPP was larger in response to snakes than lizards at frontal (Fz) and central (Cz) electrode sites, whereas no significant differences were found between angry and neutral faces. Any correlations between snake phobia symptoms and ERP responses to snake stimuli will be reported.

Conclusion
The findings suggest that snakes engage early visual and motivated attention mechanisms more strongly than angry faces, underscoring their evolutionary significance as potent fear-relevant stimuli. This distinction could inform diagnostic tools by identifying neural markers, such as exaggerated EPN or LPP responses, to assess sensitivity to specific fear triggers. Additionally, monitoring changes in these electrophysiological responses during treatment could provide objective measures of therapeutic progress in phobia and anxiety interventions.

Teleretina evaluation using autonomous methods

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Introduction

According to the CDC, nearly 1 in 3 Americans are diabetic or prediabetic, roughly 1% of Americans have glaucoma, and ARMD remains the leading cause of blindness in older Americans. To expand screening efforts, novel portable and autonomous hardware-software solutions have been developed and integrated in national health screening programs. We chose to evaluate the Phelcom Eyer AI camera for autonomous lesion detection. We tested its ability to identify lesions specific to DR, GON, and ARMD cases through a pilot study and named our project Teleretina Evaluation using Autonomous Methods (TEAMs).

Methods

A total of 130 subjects were imaged using a traditional desktop fundus camera from 2023-2024. We evaluated the identification of retinal lesions identified by dilated eye exam, fundus photography, and autonomously via an AI solution. The study protocol was approved by the Institutional Review Board of UMSL.

Results

The outcomes showed very high sensitivity scores for ARMD lesion detection (100%, n = 12), DR lesion detection (91%, n = 42). The autonomous solution was not sensitive at the detection of optic nerve pathologies, specifically GON (62%, n = 33). MRD detection was 75% (n = 10), whereby missed lesions were specific to GON.

Conclusion

Overall, the autonomous solution showed limitations specific to optic nerve disease, some of which can result in irreversible vision loss. Limiting this solution to ARMD and DR lesion detection is preferred, however, improvements to optic nerve disease detection is necessary for safe implementation and scaling.

The role of GPR68 in modulating locomotor activity and sensitization to amphetamine

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Introduction

GPR68, a proton-sensing G-protein coupled receptor (GPCR) expressed in the brain, may influence behavioral responses to stimulant drugs like amphetamine. This study investigates the role of GPR68 in modulating locomotor activity and sensitization to amphetamine by comparing acute and repeated drug exposure in GPR68 knockout (KO) and wild-type (WT) mice.

Methods

Locomotor activity was assessed in adult WT and GPR68 KO mice. After a 60-minute acclimation period, mice received daily intraperitoneal injections of amphetamine (3.0 mg/kg) for five consecutive days to evaluate initial and progressive drug responses. Following a two-week withdrawal period, a half dose of amphetamine (1.5 mg/kg) was administered to assess long-term sensitization. Locomotor activity, including total distance traveled, was recorded for 90 minutes using the VersaMax system. Genotype-specific differences were analyzed using Sigmaplot software.

Results

Preliminary data indicate that GPR68 KO mice exhibit significantly increased locomotor activity compared to WT mice following both acute and repeated amphetamine administration. This heightened activity was sustained throughout the dosing regimen and continued during the reduced-dose sensitization test.

Conclusion

The increased locomotor activity and heightened sensitivity observed in GPR68 KO mice suggest that GPR68 plays a critical role in regulating stimulant-induced behaviors. These findings highlight GPR68 as a potential therapeutic target for mitigating the effects of amphetamines and similar stimulant drugs.

Myeloid-specific leptin signaling links insulin resistance to salt-sensitive hypertension

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Introduction

Salt-sensitivity of blood pressure (SSBP) has been shown to correlate with insulin resistance, metabolic syndrome, and cardiovascular mortality. Hypertension can often be seen in settings of obesity, leptin resistance, and insulin resistance, though the exact mechanistic interaction of these conditions has yet to be elucidated. Inhibition of the mammalian target of rapamycin (mTOR), a major regulator of both insulin and leptin pathways, promotes symptoms of metabolic syndrome. We have previously shown high sodium environments activate antigen presenting cells (APCs) towards an inflammatory phenotype contributing to the pathogenesis of SSBP. In this study, we investigated whether in vitro and in vivo high sodium exposure affect leptin and insulin signaling in human monocytes.

Methods

SSBP was assessed using a modified Weinberger salt-loading and depletion protocol (age was 49.25±1.98, 80% male, screening SBP/DBP was 137.3±4/88.2±2.9). scSeq was performed on circulating immune cells. In additional experiments, bulk RNA sequencing was performed on monocytes isolated from 11 healthy individuals and were treated in vitro with either normal (150mM) or high (190mM) sodium. We analyzed the RNA sequence data and cross-referenced these results with a comprehensive list of genes associated with insulin and leptin signaling using the NIH Gene database and the Harmonizome 3.0 database.

Results

We found an overall downregulation of both insulin and leptin signaling genes. Of note, there was a significant downregulation of genes for leptin ($log2FC=-2.5$; $padj<0.0001$), leptin receptor ($log2FC=-0.53$; $padj=0.002$), insulin receptor ($log2FC=-0.36$, $padj=0.007$), and glucose transporter 1 ($log2FC=-0.74$; $padj=0.001$). Although mTOR was not significant ($log2FC=-0.07$; $padj=0.69$), proline-rich AKT1 substrate 1, a direct inhibitor of mTOR activity, ($log2FC=0.71$; $padj<0.001$), was significantly upregulated. Furthermore, we found an inverse correlation between DAKT1S1 and SSI ($r=-0.93$; $p=0.008$).

Conclusion

Our findings suggest that high salt exposed monocytes have impaired leptin and insulin signaling, which may be a factor to promote insulin and leptin resistance contributing to the development of metabolic syndrome in salt-sensitive hypertension.

Leveraging thermal gradient to investigate peripheral nerve dependent temperature behaviors in mice

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Introduction

Thermosensation is commonly dysfunctional in neurodegenerative diseases. However, recapitulating these effects in rodents has primarily relied on nociception to interpret thermosensation dysfunction. As such, our understanding of the pathomechanisms related to dysfunctional thermosensation has been limited. The somatosensory pathway of thermosensation relies on temperature-responsive potential ion channels (TRP) in peripheral neurons, which signal back to the spinal cord and the somatosensory cortex. In inherited peripheral neurodegenerative diseases and as part of aging, these TRP receptor-positive neurons degenerate, leading to altered thermosensation. Here, we use a commercially available, user-independent gradient temperature device to determine thermosensation deficits between inherited peripheral nerve and aging mouse models.

Methods

The Bio-Gradient 2.0 from Bioseb was used in this study. A temperature gradient was established across two base plates of a 120 cm long device, with a delta of 2°C over 10 virtual zones. Animals were then placed on the corridor and were free to walk in an unrestrained manner. Voluntary rodent position was recorded by video tracking software.

Results

Among inherited nerve disease mice, we found a temperature preference of 22.1°C compared to wild-type mice, who chose 26.4°C (p=0.0312). Additionally, these mice showed a reduced total distance traveled on the active device, suggesting a negative nociceptive response compared to wild type (20m vs. 37m, p=0.0101). Old mice chose significantly higher temperatures versus 6-month-old mice (32°C vs. 26.8°C, p=0.0012). There was no difference in gender between either group.

Conclusion

Here, we found that the thermal gradient sensory test was able to detect significantly different thermal behavioral responses in inherited peripheral nerve diseases and aging models. Given its reproducibility, combined with its user-independent capabilities, this device holds promise in unraveling the pathomechanisms of aberrant peripheral nerve-dependent thermosensation.

Exploring the role of GPR4 in cocaine-induced locomotor response and sensitization

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Objective

G-protein coupled receptor 4 (GPR4), which is sensitive to changes in pH, is highly expressed in the brain. This study aims to investigate the role of GPR4 in cocaine addiction by examining its effects on locomotor activity and behavioral sensitization in response to both acute and chronic cocaine exposure.

Methods

Wild-type (WT) and GPR4 knockout (KO) mice (5- to 6-month-old) were compared for locomotor activity and behavioral sensitization following saline or cocaine administration. After a 60-minute acclimation period, mice were injected with saline (10 mg/kg) or cocaine (20 mg/kg) intraperitoneally. Their locomotor activity, including total distance and stereotypy count, was monitored for 90 minutes using the VersaMax system. Following five days of repeated cocaine exposure, a two-week withdrawal period was observed before a final half-dose cocaine administration (10 mg/kg) to assess sensitization. Data was analyzed using Sigmaplot software.

Results

Preliminary data show that GPR4 KO mice exhibit a significantly greater locomotor response to both acute and chronic cocaine administration compared to WT mice. This effect was observed in both male and female GPR4 KO mice, with a more pronounced increase in response and sensitization in females. Both total distances traveled, and stereotypy activity revealed congruent differences between genotypes.

Conclusion

The increased locomotor response and sensitization to cocaine observed in GPR4 KO mice suggest that GPR4 may play a protective role in cocaine addiction. These findings highlight GPR4 as a potential target for future therapeutic interventions in substance use disorders. Additionally, the observed gender differences in response to cocaine in GPR4 KO mice warrant further investigation.

Impact of homelessness on 30-day readmission in patients undergoing lower extremity bypass

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Introduction
Patients experiencing homelessness face a multitude of health-related challenges that increase risk of morbidity and mortality. Few reports have assessed the impact of housing status on vascular surgical outcomes. We aimed to identify risk factors, including homelessness, for 30-day readmission among adults undergoing open lower extremity (LE) bypass procedures.

Methods
In this retrospective cohort study, patients undergoing open LE bypass procedures from 2018 to 2020 from the Nationwide Readmissions Database were queried using ICD-10 procedure and diagnosis codes. Chi-squared test and t-test were used for categorical and continuous variables, respectively. Multiple logistic regression was used to identify factors associated with 30-day readmission.

Results
58,082 patients underwent open LE bypass, of which 10,683 patients were readmitted within 30 days (18.4%). Readmitted patients tended to be older, female, below the 25th percentile in median household income, and had a higher rate of comorbidities including cerebrovascular disease, chronic pulmonary disease, congestive heart failure, and renal disease ($p<0.01$). Readmitted patients were also more likely to be homeless, have a greater length of stay, and receive amputations compared to non-readmitted patients ($p<0.01$). In multiple logistic regression, female sex (OR 1.16, 95% CI 1.11—1.21), homelessness (OR 1.65, 95% CI 1.25—2.16), increased illness severity (OR 2.34, 95% CI 2.17—2.52), amputation (OR 1.10, 95% CI 1.02—1.20) and hemorrhage as a complication (OR 1.09, 95% CI 1.03—1.14) were associated with higher odds of readmission.

Conclusion
Homeless patients undergoing open LE bypass may be at increased risk for readmission to the hospital within 30 days. Thus, housing instability may be associated with increased morbidity and financial burden to the healthcare system. This data highlights the impact of homelessness on vascular surgical outcomes and overall hospital system utilization.

Multiple isoforms of RNA-binding protein Bruno1 are required during indirect flight muscle development in Drosophila

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Objective

During development, indirect flight muscles (IFMs) of Drosophila undergo a switch in fiber-type specific alternative splicing that is essential for flight behavior. This switch is regulated by RNA-binding proteins (RBPs), especially Bruno1 (Bru1). Bru1 is a conserved member of the CELF family, which are important regulators of developmental alternative splicing in vertebrate striated muscle. CELF activity is misregulated in patients with Myotonic Dystrophy Type I, notably resulting in a reversion to embryonic splicing patterns and indicating that CELF function is critical to muscle development. Bru1 is alternatively spliced to produce at least 6 protein isoforms, but isoform-specific CELF functions are not reported in flies or vertebrates. In flies, Bru1 is known to play a role in translation repression during embryo formation, but recent work identified Bru1 as a muscle fiber-type specific splicing factor which is necessary for IFM-specific splice isoforms. Bru1 promotes early cytoskeletal rearrangements enabling myofibrillogenesis and later promotes maturation of the sarcomeres and contractility.

Methods

Using Gal4-UAS to control when and where specific Bru1 isoforms are expressed, we test the function of long (isoform B), middle (isoform A), and short (isoform D) isoforms. Our results show distinct localization patterns for Bru1 isoforms. Using Him-Gal4 and Fln-Gal4 to drive early and late overexpression during myofibrillogenesis.

Results

We show that overexpression of Bru1-isoB results in a strong muscle detachment phenotype, while Bru1-isoA overexpression disrupted sarcomere structure. This phenotype is dosage dependent, and we use temperature shifting and alternate UAS promoters to modulate Bru1 expression levels. Bru1-isoD overexpression resulted in only minor muscle defects. We further tested isoform-specific rescue ability and found that a combination of Bru1-isoA and Bru1-isoD are required to rescue IFM development.

Conclusion

These differences suggest a requirement for distinct Bru1 isoforms during muscle development and are the first demonstration of CELF-family isoform-specific function in myogenesis.

Understanding Risk Factors and Their Association with Optic Neuropathy

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Objective

Optic neuropathy is a debilitating condition characterized by damage to the optic nerve, leading to vision loss. Understanding the associations between comorbidity conditions and optic neuropathy is essential for improving patient outcomes. This study uses a deidentified Electronic Health Records (EHR) dataset to evaluate demographic and clinical predictors of optic neuropathy using a logistic regression model.

Methods

A retrospective cohort of 5,499 individuals was analyzed. Age distribution was categorized as <50 (2,621), 51–65 (1,102), 66–80 (1,089), and >80 (687). Based on the Charlson comorbidity index with adjusted weight, comorbidity conditions were assessed using variance inflation factor (VIF) analysis to avoid multicollinearity. Logistic regression was performed, with optic neuropathy as the dependent variable. Model performance was evaluated using precision, recall, and F1-score metrics. The final model's confusion matrix and classification report were examined for predictive accuracy.

Results

Key predictors of optic neuropathy included hemiplegia/paraplegia (OR = 1.94, $p < 0.001$), hypertension (OR = 2.71, $p < 0.001$), cerebrovascular disease (OR = 2.12, $p = 0.001$), chronic pulmonary disease (OR = 3.18, $p < 0.001$), and diabetes with chronic complications (OR = 2.47, $p < 0.001$). The logistic regression model achieved 85% accuracy, with a weighted F1-score of 0.82. However, convergence issues were noted, indicating potential quasi-separation.

Conclusion

This retrospective study using EHR data identifies significant associations between specific comorbidity conditions and optic neuropathy. Hypertension, chronic pulmonary disease, and diabetes with chronic complications were shown as strong predictors. Despite the model's solid predictive performance, further analysis is needed to address convergence limitations and validate findings. These results underscore the importance of comprehensive management of systemic conditions in patients at risk for optic neuropathy, highlighting the importance of ongoing research in this field.