Concussion Tests: MedlinePlus Lab Test Information

What are concussion tests?

Concussion tests can help find out if you or your child has suffered a concussion. A concussion is a type of brain injury caused by a bump, blow, or jolt to the head. Young children are at a higher risk of concussions because they are more active and because their brains are still developing.

Concussions are often described as mild traumatic brain injuries. When you get a concussion, your brain shakes or bounces inside your skull. It causes chemical changes in the brain and affects brain function. After a concussion, you may have headaches, mood changes, and problems with memory and concentration. The effects are usually temporary, and most people make a full recovery after treatment. The main treatment for a concussion is rest, both physical and mental. Left untreated, a concussion can cause long-term brain damage.

Other names: concussion assessment

What are they used for?

Concussion tests are used to assess brain function after a head injury. A type of concussion test, called a baseline test, is often used for athletes who play contact sports, a common cause of concussion. A baseline concussion test is used on non-injured athletes before the start of a sports season. It measures normal brain function. If a player gets injured, the baseline results are compared with the concussion tests performed after the injury. This helps the health care provider see if the concussion has caused any problems with brain function.

Why do I need concussion testing?

You or your child may need concussion testing after a head injury, even if you think the injury is not serious. Most people don’t lose consciousness from a concussion. Some people get concussions and don’t even know it. It’s important to watch for concussion symptoms so you or your child can get treated promptly. Early treatment can help you recover faster and prevent further injury.

Concussion symptoms include:

Some of these concussion symptoms show up right away. Others may not show up for weeks or months after the injury.

Certain symptoms may mean a more serious brain injury than a concussion. Call 911 or seek immediate medical attention if you or your child has any of the

following symptoms:

- Inability to be woken up after injury
- Severe headache
- Seizures
- Slurred speech
- Excessive vomiting

What happens during concussion testing?

Testing usually includes questions about concussion symptoms and a physical exam. You or your child may also be checked for changes in:

- Vision
- Hearing
- Balance
- Coordination
- Reflexes
- Memory
- Concentration

Athletes may get concussion baseline testing before the start of a season. A baseline concussion test usually involves taking an online questionnaire. The questionnaire measures attention, memory, speed of answers, and other abilities.

Testing sometimes includes one of the following types of imaging tests:

In the near future, a blood test may also be used to help diagnose a concussion. The FDA recently approved a test, called the Brain Trauma Indicator, for adults with concussions. The test measures certain proteins that are released into the bloodstream within 12 hours of a head injury. The test may be able to show how serious the injury is. Your provider may use the test to decide whether or not you need a CT scan.

Will I need to do anything to prepare for a concussion test?

You don’t need any special preparations for concussion testing.

Are there any risks to the tests?

There is little risk to having concussion testing. CT scans and MRIs are painless, but can be a little uncomfortable. Some people feel claustrophobic in an MRI scanning machine.

What do the results mean?

If your results show that you or your child has a concussion, rest will be the first and most important step in your recovery. This includes getting

plenty of sleep and not doing any strenuous activities.

You'll also need to rest your mind too. This is known as cognitive rest. It means limiting schoolwork or other mentally challenging activities, watching TV, using the computer, and reading. As your symptoms improve, you can gradually increase your level of physical and mental activities. Talk to your health care provider or your child's provider for specific recommendations. Taking enough time to recover can help ensure a full recovery.

For athletes, there may be specified steps, called a concussion protocol, that are recommended in addition to the steps listed above. These include:

- Not returning to the sport for seven or more days
- Working with coaches, trainers, and medical professionals to assess the athlete's condition
- Comparing baseline and after-injury concussion results

Is there anything else I need to know about concussion testing?

There are steps you can take to prevent concussions. These include:

- Wearing helmets while biking, skiing, and doing other sports
- Regularly checking sports equipment for proper fit and function
- Wearing seatbelts
- Keeping the home safe with well-lit rooms and removing objects from floors that might cause someone to trip. Falls in the home are a leading cause of head injury.

Preventing concussions is important for everyone, but it's especially crucial for people who have had a concussion in the past. Having a second concussion close to the time of the first injury can cause additional health problems and lengthen recovery time. Having more than one concussion in your lifetime may also cause some long-term health problems.

Mental Health Symptoms Common After Mild Brain Injury

WEDNESDAY, March 6, 2019 — Approximately one in five individuals may develop mental health symptoms up to six months after mild traumatic brain injury (mTBI), according to a study recently published in *JAMA Psychiatry*.

Murray B. Stein, M.D., M.P.H., from the University of California in San Diego, and colleagues evaluated the prevalence of and risk factors for

posttraumatic stress disorder (PTSD) and major depressive disorder (MDD) among 1,155 patients seen in the emergency department for mTBI versus 230 patients with nonhead orthopedic trauma injuries. Patients (≥17 years) were treated in 11 U.S. hospitals with level 1 trauma centers.

The researchers found that at three months, the weights-adjusted prevalence of PTSD and/or MDD in the mTBI group was 20.0 percent versus 8.7 percent in the orthopedic trauma comparison group. Findings were similar at six months (21.2 versus 12.1 percent). Lower education (adjusted odds ratio [aOR], 0.89 per year), being black (aOR, 5.11), self-reported psychiatric history (aOR, 3.57), and injury resulting from assault or other violence (aOR, 3.43) were risk factors for probable PTSD at six months after mTBI. For probable MDD after mTBI, similar risk factors were seen, except for cause of injury.

“We are seeing more evidence about the need to monitor these individuals for many months after their injury to help them achieve the best recovery possible,” a coauthor said in a statement.

Abstract/Full Text (subscription or payment may be required)

Posted: March 2019

Using steroids during cardic bypass surgery did not reduce acute kidney injury risk

Using steroids during cardiopulmonary bypass surgery did not reduce the risk of acute kidney injury in people at increased risk of death, according to a study conducted in 18 countries published in *CMAJ* (*Canadian Medical Association Journal*) http://www.cmaj.ca/lookup/doi/10.1503/cmaj.181644.

The multisite randomized controlled trial, funded by the Canadian Institutes of Health Research, included patients in Canada, China, India, United States, Colombia, Australia, Italy, Iran, Czech Republic, Greece, Spain, Brazil, Austria, Belgium, Hong Kong, Argentina, Chile and Ireland, which broadens the reach of the study’s findings.

About one-fifth of the millions of bypass surgeries performed around the

world each year result in acute kidney injury, which in its most severe forms greatly increases the chance of death and the need for life-sustaining dialysis treatments. Bypass surgery can trigger widespread inflammation, which is thought to be a key culprit in the development of kidney injury. Prior studies suggested that steroids might help reduce inflammation and acute kidney injury.

“Administering steroids to prevent inflammation during surgery did not reduce the risk of acute kidney injury in people at moderate or high risk of adverse effects,” says author Dr. Amit Garg, a scientist at Lawson Health Research Institute and professor at Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada.

The study included 7286 patients, of whom about half (3647) were randomized to receive steroids and the remaining 3639 to placebo. The rate of acute kidney injury was similar in both groups.

“Given the broad range of countries and populations represented in the study, these findings further support a shift away from using steroids as an effective method of preventing the complications from inflammation during bypass surgery,” states Dr. Garg.

Peripheral nerve injury can trigger the onset and spread of ALS, shows study

A growing collection of anecdotal stories raises the possibility that nerve injury in an arm or a leg can act as a trigger for the development amyotrophic lateral sclerosis, or ALS – a progressive neurodegenerative disease also known as Lou Gehrig’s disease, named after the famous New York Yankee who died of it in 1941.

The connection between ALS and athletes runs deeper than a single ballplayer; people who engage in intense physical activities, such as professional athletes and people in the military, are more likely to be affected by ALS. In some, the disease seems to start after an injury – muscle weakness at the site of the injury slowly spreads to new areas until weakness in the muscles responsible for breathing causes suffocation.

Now, researchers at the University of Illinois at Chicago are the first to demonstrate that a peripheral nerve injury can trigger the onset and spread of the disease in an animal model of ALS. Their findings, published in the journal *Neurobiology of Disease*, show that rats genetically engineered to develop ALS-like symptoms have an abnormal inflammatory response in the region of the spinal cord associated with an injured peripheral neuron. As

the spinal cord inflammation and other damaging processes spread, they cause progressive muscle weakness throughout the body.

“We know that in some patients with ALS the weakness starts in a hand or leg, and the disease spreads. Coincidentally, the patient will describe a recent or remote injury to that same hand or leg that matches the location of their disease onset. We wanted to study how environmental contributions, such as a focal nerve injury, affects how the ALS starts and spreads,” said Dr. Jeffery Loeb, the John S. Garvin Endowed Chair in Neurology and Rehabilitation in the UIC College of Medicine and corresponding author of the paper.

“Our results show that a single nerve injury, which is small enough that it only causes temporary weakness in normal animals, can start a cascade of inflammation in the spinal cord that initiates and causes the disease to spread in genetically-susceptible animals,” said Loeb. “The ability to precipitate the disease through injury gives us a new animal model we can use to identify treatments for ALS that focus on stopping the spread of the disease after it first starts. The medical community has no therapies that significantly slow or stop the progression of the disease and we are currently putting all of our efforts on developing a drug to do this.”

While a growing number of genes have been associated with the development of ALS, only about 10 percent of ALS patients have one or more of these gene mutations and none can explain why the disease presents with localized weakness or how it spreads. Ninety percent of ALS patients develop the disease for unknown reasons.

“This raises an important question of the relative contributions of environment versus genes or nature versus nurture,” Loeb said.

One of the most highly-studied gene mutations in ALS is in a gene called SOD1. In their study, Loeb and colleagues used rats with mutated forms of the SOD1 gene, which causes the animals to have higher levels of the SOD1 enzyme and to develop ALS-like symptoms, including progressive muscle weakness, starting at 15 weeks of age.

The researchers surgically injured a single nerve in the leg of both SOD1 and wild-type rats at 10 weeks of age. While all rats had reduced strength in the injured leg post-surgery, the wild-type rats recovered almost completely within a few weeks. The SOD1 rats never returned to normal and also experienced weakness in their other leg.

They also found that surgically-injured rats had elevated and prolonged inflammation, and higher numbers of microglia and astrocyte cells in areas of the spinal cord associated with the injured neuron, and the inflammation and presence of these other cells spread to adjacent neurons.

“This spread of inflammation could potentially explain how the disease spreads once it first starts from the site of injury,” Loeb said. “Microglia have many roles, but one role is to prune or eliminate synapses that connect one nerve cell to another. These connections are critical for normal functioning and for survival of neurons during development. Where there was

increased inflammation and microglia in the spinal cord, we saw up to a two-fold reduction in the number of synapses."

Loeb explained that once a nerve loses connections with its neighbors, the neighboring cells tend to die off.

"This chain reaction of cell death could be what causes the progressive spread of muscle weakness we see in ALS," Loeb said.

Source:

Can a nerve injury trigger ALS?

New target could help protect vision following optic nerve trauma

Dr. Abdelrahman Y. Fouda, Dr. Ruth B. Caldwell and research associate Zhimin Xu. Credit: Phil Jones, Augusta University Senior Photographer

When a car crash or explosion results in an optic nerve injury, eliminating an enzyme known to promote inflammation appears to aid recovery, scientists

report.

They have shown for the first time in a mouse model of tough-to-treat optic nerve trauma, that removing the enzyme arginase 2, which increases with injury, decreases neuron death in the retina as well as the degeneration of nerve fibers that connect neurons to each other and ultimately the brain, they report in the journal *Frontiers in Neuroscience*.

“Right now when an optic nerve crush injury happens, there is not a lot we can do to help the eye recover,” says Dr. Ruth B. Caldwell, cell biologist in the Vascular Biology Center at the Medical College of Georgia at Augusta University.

“We know we can’t prevent the initial damage, there is going to be some acute injury, but what deleting this enzyme seems to do is prevent subsequent amplification of the original injury. Collateral damage is less,” says Caldwell, the study’s corresponding author.

The findings elucidate both the role A2 plays in retinal damage following trauma and highlight A2’s potential as a logical treatment target, the scientists write.

The optic nerves connect the eyes to the brain and collect impulses the retina generates from light so that we can see. There is currently no therapy that targets optic nerve trauma largely because understanding of all the damaging players is unclear, they write.

While little also is known about A2’s normal function, it appears to be the polar opposite of arginase 1, an enzyme key to helping our liver eliminate ammonia. As the scientists recently found, A1 can suppress destructive inflammation that results when conditions like diabetes and glaucoma reduce blood flow to the retina. When A1 levels decrease, which they are finding happens in a variety of types of eye injuries, A2 levels increase and so do inflammation and damage.

In their model of optic nerve injury, they again found increased A2 expression after the injury and that neurons in the retina as well as retinal ganglion cells, the primary cell type in the optic nerve, began to die. While some death of retinal ganglion cells obviously occurs immediately following this type injury, destruction can continue out seven days or more, the scientists say.

Higher A2 also increased glial cell activation following injury. Glial cells are a different type brain cell that nourish and otherwise support neurons. But when they are activated, they forgo their supportive role, Caldwell says.

The destructive results turned around, when they removed A2 from the equation. Neuron loss diminished as did the degeneration of nerve fibers, called axons that connect retinal ganglion cells to the brain, and glial activation was reduced. There were other signs of support, like an increase in brain derived neurotrophic factor, also known to support the survival of neurons and axons.

“We are showing for the first time that there is a connection between brain derived neurotrophic factor and arginase 2,” says Dr. Abdelrahman Y. Fouda, postdoctoral fellow in Caldwell’s lab and a study coauthor.

They even saw some axons sprouting past the point of the crush injury, Fouda says.

“We have some evidence that possibly the axons are trying to repair themselves,” Caldwell adds of these early indicators of the neurons’ ability to reconnect with each other and ultimately the brain. “It looks like they are trying to get there,” she says, “but we have a lot more work to do to prove that.”

There also was more growth associated protein 43, or GAP43, which is known to help axons regenerate. In fact, the scientists found one way brain derived neurotrophic factor may benefit the optic nerve is by, in turn, helping increase the levels of GAP43. A2 deletion also inhibited injury associated-increases in inflammation-promoting immune cells like interleukin.

“We have already seen A2 go up in other types of injury,” says Caldwell, referencing problems that also include retinal damage that occurs in premature babies as well as the ischemic retinopathy found in conditions like diabetes.

“What we know now is that when we delete A2, it makes recovery better from an optic nerve crush,” Caldwell says.

To date in all their models, which now include optic nerve trauma, when A2 levels go up, A1 goes down.

They suspect that by giving a more stable but still human grade of A1, as they already are doing in other eye injury models, it will help drive down A2 in optic nerve crush injury as well, and are pursuing this and other lines of investigation.

New treatment target emerging for retinal damage

More information:
Frontiers in Neuroscience (2019). www.frontiersin.org/articles/1 … nins.2018.00970/full

Provided by
Medical College of Georgia at Augusta University

Citation:
New target could help protect vision following optic nerve trauma (2019, February 11)

New target appears to aid recovery after optic nerve trauma

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investigation.

Source:

https://www.augusta.edu/mcg/

Specific cognitive deficits found in individuals with spinal cord injury

Similarities in cognitive findings between persons with spinal cord injury and older healthy individuals could indicate accelerated aging of the brain after spinal cord injury

A multidisciplinary team of researchers has identified specific cognitive deficits in individuals with spinal cord injury (SCI). Their findings support the theory of accelerated aging after SCI, and have important implications for further research.

The article, "Patterns of cognitive deficits in persons with spinal cord injury as compared with both age-matched and older individuals without spinal cord injury", (doi: 10.1080/10790268.2018.1543103) was epublished ahead of print on December 3, 2018 by the *Journal of Spinal Cord Medicine*. The authors are scientists with expertise in cognitive rehabilitation and SCI rehabilitation: Nancy D. Chiaravalloti, PhD, Erica Weber, PhD, Glenn Wylie, DPhil, and Trevor Dyson-Hudson, MD, from Kessler Foundation, and Jill M. Wecht, EdD, from the James J. Peters VA Medical Center.

Courtesy of the publisher, this article is Open Access through March 31. https://doi.org/10.1080/10790268.2018.1543103

Individuals with chronic SCI have an increased risk for cognitive impairment, which can adversely affect recovery and overall quality of life. Concomitant brain injury fails to account for the increased risk for cognitive deficits. Multiple factors contribute to the high incidence – up to 60 percent demonstrate some degree of cognitive impairment.

Developing effective interventions is dependent on precise knowledge of the types of deficits. To explore this question, the team administered a battery of neuropsychological tests to 3 groups: 60 individuals with spinal cord injury (32 paraplegia, 28 tetraplegia), 30 age-matched controls, and 20 older healthy controls. None of the tests required motor ability; these included the WAIS-III Digit Span and Letter-Number Sequencing; Symbol Digit Modalities Test (SDMT) – oral version; California Verbal Learning Test-II; Paced Auditory Serial Addition Test (PASAT); the Wechsler Abbreviated Scale of

Intelligence (WASI); Delis-Kaplan Executive Function System; and the Verbal Fluency subtest.

Significant differences were found between the SCI group and the age-matched control group, according to Dr. Chiaravalloti, director of Traumatic Brain Injury (TBI) Research, and director of the Northern New Jersey TBI Model System. “The individuals with SCI had deficits in information processing speed, verbal fluency, and new learning and memory,” noted Dr. Chiaravalloti, “while their attention and working memory were unaffected. As we had postulated, their neuropsychological profile more closely aligned with that of older healthy controls. This could be a sign of accelerated brain aging after SCI, a phenomenon that has been associated with other neurological conditions.”

“People often focus on mobility impairments associated with SCI; however, addressing cognitive deficits in this population is also critically important,” said co-author Dr. Dyson-Hudson, director of SCI Research, and director of the Northern New Jersey SCI Model System. “Future research needs to be based on broader measures of neuropsychological function. Identifying modifiable risk factors and developing targeted cognitive interventions will help restore maximal function, and support the efforts of individuals to participate in their communities and the workforce.”

Source:

http://www.kesslerfoundation.org/content/researchers-identify-specific-cognitive-deficits-individuals-spinal-cord-injury

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Study links concussions to development of epilepsy

Altered astrocytes may be the root of epilepsy development

Researchers at the Fralin Biomedical Research Institute at VTC have identified a cellular response in mice to mild traumatic brain injuries that may lead to seizures.

Traumatic brain injury is a leading cause of epilepsy, which is characterized as the repeated occurrence of seizures. No treatments currently interrupt the process that the brain undergoes after injury that can eventually lead to the chronic condition of epilepsy.

The study, published today in *JNeurosci*, suggests that the development of epilepsy triggered by mild traumatic brain injury may be related to an

atypical response from brain cells known as astrocytes, which change to form scars after a severe brain injury. This process is important to protect uninjured brain areas but comes at a price, because these scars have been associated with epilepsy.

The scientists found that astrocytes do not form scars after mild traumatic brain injury, but some astrocytes are altered in a different way almost immediately by these less severe types of injuries. Then, weeks later, the scientists observed spontaneous, recurrent seizures in some mice.

“Our experiments show a strong relationship between changes in astrocytes and the eventual occurrence of a seizure,” said Stefanie Robel, the corresponding author of the study, who is an assistant professor with the Fralin Biomedical Research Institute and at the School of Neuroscience in Virginia Tech’s College of Science. “The findings point to a unique population of astrocytes that respond within 30 minutes of an injury being at the root of a problem where seizures may occur after a latency period of weeks or months, suggesting a therapeutic window to prevent seizure disorders after concussive injuries.”

Robel, research associate Oleksii Shandra, and colleagues at the Fralin Biomedical Research Institute discovered areas of the brain where astrocytes no longer performed their usual housekeeping work to support normal nerve cell function after mild traumatic brain injury.

They first assumed these pockets of nonfunctioning astrocytes were dead, because they no longer made the proteins that normally identify them as astrocytes. Later, Alex Winemiller, a research assistant at the Robel lab and one of the first authors of the study, discovered the cells were alive, but not reacting to injury in their typical manner.

Researchers compared data from mice that eventually developed epilepsy with mice that never developed seizures and found a correlation between the loss of function in patches of astrocytes and the development of epilepsy.

“Each of these astrocytes is connected to multiple neurons, which make hundreds of thousands of connections, which means the loss of function of even a few astrocytes can be devastating to other cells in the brain,” said Shandra, the first author of the study. “Not only have these astrocytes lost their function, but due to these altered connections, the effects can be widespread to brain cells far away. The degree of this astrocyte dysfunction might be something that defines whether epilepsy develops.”

While it has been known that traumatic brain injury is a leading cause of acquired epilepsy, the precise relationship between such injuries and seizures has been elusive.

This new study shows that after a latency period, some of the mice developed spontaneous recurrent seizures reminiscent of post-traumatic epilepsy in human patients with traumatic brain injuries, providing a new experimental model that could contribute to understanding of post-traumatic epilepsy.

Source:

https://research.vtc.vt.edu/news/2019/jan/21/fralin-biomedical-research-institute-scientists-li/

FSU study provides better understanding of spinal cord injuries

Thousands of people worldwide suffer severe spinal cord injuries each year, but little is known about why these injuries often continue to deteriorate long after the initial damage occurs.

Yi Ren, a professor of biomedical sciences at the Florida State University College of Medicine, is making progress in understanding why such significant harm is inflicted in the weeks and months after a spinal injury. In a study published today in the journal *Nature Neuroscience*, Ren explained how a natural immune system response may contribute to additional injury.

When spinal cord damage occurs, the endothelial cells that line blood vessels are activated to remove potentially harmful material, like myelin debris, from the site of the injury. However, Ren and her team discovered that this process may be responsible for causing further harm.

“The consequences of the effort of endothelial cells to clear myelin debris is often severe, contributing to post-traumatic degeneration of the spinal cord and to the functional disabilities often associated with spinal cord injuries,” said Ren, whose team conducted the study over a period of five years.

Myelin debris at the injury site comes from a shattering of the insulation protecting axons – the central nervous system’s primary transmission lines.

The inflamed area fills with macrophages, a type of white blood cell that engulfs foreign material and dead cells and is a key player in the immune response system. Macrophages remain in the area of the inflammation for months or even years. The mechanisms for macrophage infiltration remain unclear.

“Uncontrolled inflammation is one of the most important pathological events in the secondary injury cascade,” Ren said. “It persists for a long period of time following a spinal cord injury. We know that myelin debris acts as an inflammatory stimulus that exacerbates secondary injury by activating other cells in the injured spinal cord that are actively involved in inflammatory responses during disease progression.

“Clearing myelin debris generated at the time of injury is critical in controlling the inflammatory response and to ensuring neural regeneration.”

Little is known about the cellular and molecular mechanisms at work in clearing myelin debris from the injury site.

Ren’s lab demonstrated that debris can be engulfed by blood vessels and endothelial cells in the injured spinal cord. The problem is that once endothelial cells engulf the debris, they are enabled to promote inflammation and the formation of abnormal blood vessels. Those outcomes would inhibit the chances of a full recovery.

“Unexpectedly, we found that the process of engulfing debris confers upon endothelial cells the ability to stimulate production of fibrotic components suggesting that these cells have a function in the formation of fibrotic scars,” Ren said. “Specifically, they facilitate the arrival of macrophages derived from bone marrow that ultimately promote chronic inflammation.”

Ren said the same findings apply to the central nervous system damage inflicted by multiple sclerosis.

With a better understanding of the mechanisms at work, Ren hopes that researchers will find new ways for accident victims to regain lost functional ability without many of the unwanted side effects.

Source:

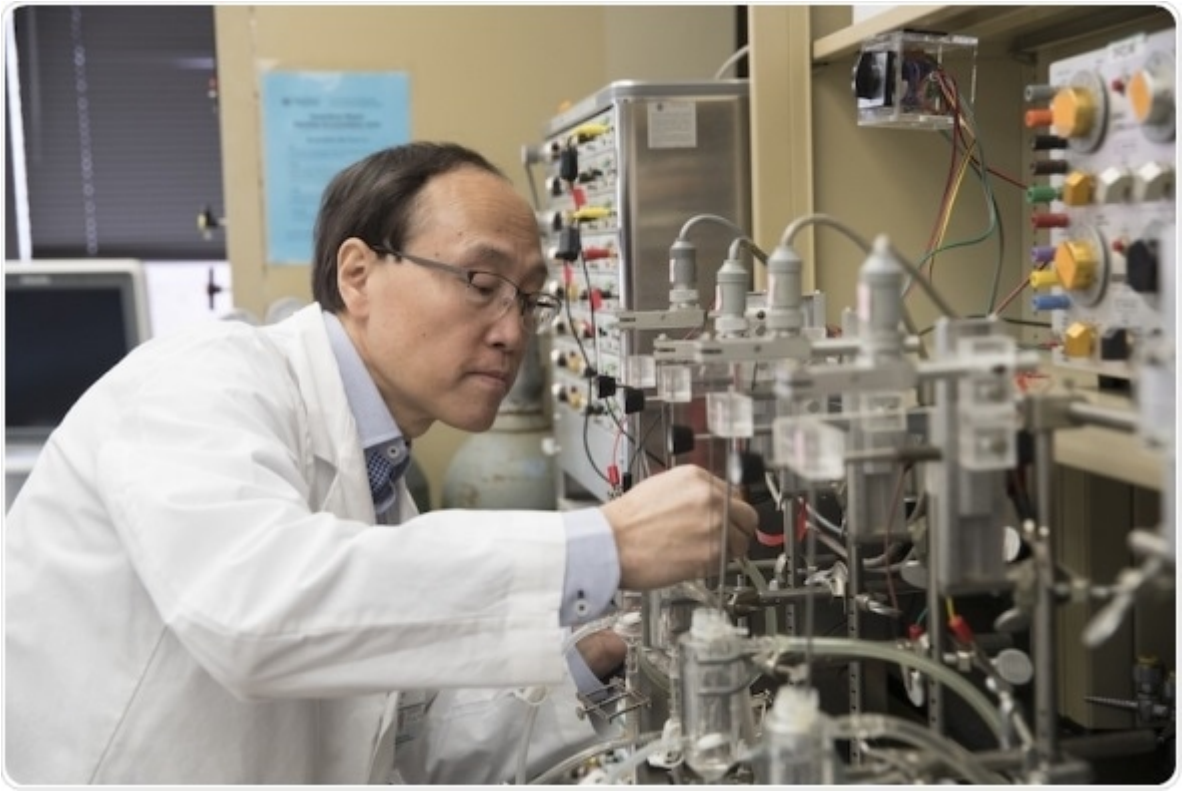
FSU research sheds light on spinal cord injuries

Pre-injury exercise reduces damage to both muscles and nerves, study finds

Jan 17 2019

Exercise Expert Seeks to Prevent Damage Caused by Restoration of Blood Flow

Exercise can protect both muscle and nerves from damage caused by the restoration of blood flow after injury or surgery, new research from the University of Virginia School of Medicine shows.



UVA's Zhen Yan, PhD, is a top expert on the cellular benefits of exercise. He is working to overcome the problem of ischemia reperfusion injury, in which the body is damaged by the restoration of blood flow after it has been cut off by injury or surgery.

UVA's Zhen Yan, PhD, a top expert on the cellular benefits of exercise, and his team are working to better understand how the body is damaged by the restoration of blood flow – known as ischemia reperfusion injury – and to find ways to improve outcomes for people who suffer it, including surgery and trauma patients and soldiers injured on the battlefield. Their new finding shows that pre-injury exercise has substantial benefits in terms of preserving both muscle and nerve.

"Exercise-trained mice had a much better recovery, evidenced by less nerve damage, less muscle damage and less reduction of contractile function [in the muscle] immediately after injury and days later," explained Yan, the director of the Center for Skeletal Muscle Research at UVA's Robert M. Berne Cardiovascular Research Center.

The Danger of Ischemia Reperfusion Injury

Because of the damage caused by reperfusion injury, doctors now seek to limit the amount of time blood flow is cut off to no more than 90 minutes.

> There are some situations where you have to stop bleeding to save life. The way we often do that is by putting on a tourniquet, to completely stop the circulation until the patient can be taken to

> the emergency room. But there's an issue there: We cannot block it too long. The tissues will be dead. We have to restore the blood flow at some point, but it will cause reperfusion injury. There is a conundrum."
>
> Zhen Yan, PhD, UVA

In his latest research, Yan and his team used a "reporter gene" he developed called the MitoTimer to understand the effects of reperfusion injury on muscle and nerves. The reporter gene allowed them to measure the amount of "oxidative stress" to the cells' powerplants, mitochondria, when blood flow was restored.

They found that pre-injury exercise clearly reduced the damage to both muscle and nerve, but it did not significantly reduce the amount of oxidative stress.

> We know exercise made the muscle and nerve tougher. The protection is very clear."
>
> Zhen Yan, PhD, UVA

While the mechanism for that protection is not yet understood, Yan's previous research has shed light on what happens to muscle cells when blood flow is restored. He likens it to wires being disconnected from a circuit board. He's even identified a compound that, in mice, helps protect the mitochondria in those circuit boards. "With this treatment, we found the circuit board, a structure called neuromuscular junction where nerve is physically connected with muscle for control of its contraction, was preserved," he said. "The wires remained connected. The function is normal. Therefore, recovery is much faster." This drug could potentially prevent nerve damage caused by the restoration of blood flow and speed patients' recovery. (It is clear, however, that exercise training achieves this through a different mechanism.)

More work will need to be done before such a drug could be used in humans, but Yan thinks the discovery holds great promise. He envisions that the drug could be of tremendous use to the military, for example.

> On the battlefield, a simple thing to do is to put a bandage around the limb to block the circulation, to block the bleeding. But at a certain point, you have to re-establish circulation, and our approach could offer a way to minimize the collateral damage and get better outcomes."
>
> Zhen Yan, PhD, UVA

Yan, of UVA's Division of Cardiovascular Medicine, plans to continue his investigation into both the drug and reperfusion injury in general as part of

his larger studies into how exercise benefits our cells and human health.

Source:

https://newsroom.uvahealth.com/2019/01/15/exercise_protects_muscles_nerves/

New NSF funded study may help physicians decrease brain injury deaths

To help physicians decrease the number of deaths resulting from traumatic brain injuries, Chandan Reddy, associate professor in the Department of Computer Science and faculty at the Discovery Analytics Center, will use new machine learning techniques for computational models to predict short- and long-term outcomes, categorize traumatic brain injury patients, and provide interventions tailored to a specific patient and his or her injury. This four-year study is funded by a National Science Foundation grant in excess of $1 million.

Traumatic brain injury affects more than 10 million people worldwide and is a leading cause of death in the United States for children and adults under the age of 44.

“While nothing much can be done to change a primary brain injury, there is room to prevent further damage to the brain,” said Reddy. The overall goal of the project is to provide insights into what might happen next, like increased intracranial pressure and metabolic derangement, by using novel computational algorithms. This information can help physicians focus on detecting and preventing these kinds of secondary injuries.

One of the bigger challenges for physicians is that no two brain injuries are alike, even when the circumstances seem identical.

“Our research is especially important because it goes beyond general possibilities to the more specific ones,” Reddy said.

Data sources for the study will include inpatient bedside data, as well as remotely monitored telemedicine data, providing the ability to connect data at multiple levels for specific patient populations.

Reddy is working with Vignesh Subbian, assistant professor in the Department of Biomedical Engineering and the Department of Systems and Industrial Engineering at the University of Arizona. The study is also receiving some assistance from clinical experts from the University of Cincinnati and Emory

University.

The tools developed through this research will help critical care physicians and clinicians provide the right care to each patient and better select patients for appropriate brain injury-related clinical trials.

“This work has a strong potential for application in broader contexts within the health care industry by helping families with decision-making about long-term care and by potentially informing ways to reduce overall healthcare and societal costs for this patient population as well,” Reddy said.

Through outreach and educational activities, the project will also promote awareness of computational methods and systems among graduate and undergraduate students, along with clinical trainees.

Source:

https://vtnews.vt.edu/articles/2019/01/virginia-tech-professor-uses-new-machine-learning-techniques-to-0.html

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Review highlights calcium handling mechanisms involved in reperfusion injury

Stroke and myocardial infarction (MI) are a significant cause of death and disability worldwide. However, over the past several decades because of advances in medicines (thrombolytic agents, antiplatelet drugs, beta blockers, and angiotensin converting enzyme inhibitors) and approaches to restore tissue perfusion (percutaneous coronary intervention and cardiopulmonary bypass), the mortality of MI has declined dramatically.

These treatments have been known to reduce acute myocardial ischemic injury and to limit MI size when experiments and were done on animals. However, reperfusion can itself amplify cell injury and death; this is known as myocardial ischemia-reperfusion injury (I/R). Several studies have uncovered complex mechanisms of cardiomyocyte damage after the process of reperfusion, and efforts are ongoing to search for therapeutic targets to reduce I/R. One of the most observations is is the elevation of Ca^{2+} ions that takes place at intracellular and mitochondrial levels during reperfusion. This increase in Ca^{2+} predisposes patients to mitochondrial failure, hyper-contracture and proteolysis, eventually leading the cell toward necrotic or apoptotic death. The channels of the sarcolemma (L-Type Ca^{2+} channels and sodium/calcium exchangers), the endoplasmic/sarcoplasmic reticulum (SERCA ATPase) and

ryanodine receptors, SOCE(store-operated calcium entry), lysosomes and others, which are modified by I/R injury are responsible for these enormous alterations in cytosolic Ca2+ levels.

This review describes different biochemical pathways that lead to Ca2+ overload that causes I/R. Advances in therapeutic strategies oin light of recent discoveries are also discussed.

Source:

https://benthamscience.com/

Posted in: Medical Science News | Medical Research News

Tags: Angiotensin, Calcium, Cell, Disability, Drugs, Enzyme, Intracellular, Light, Lysosomes, Mortality, Stroke

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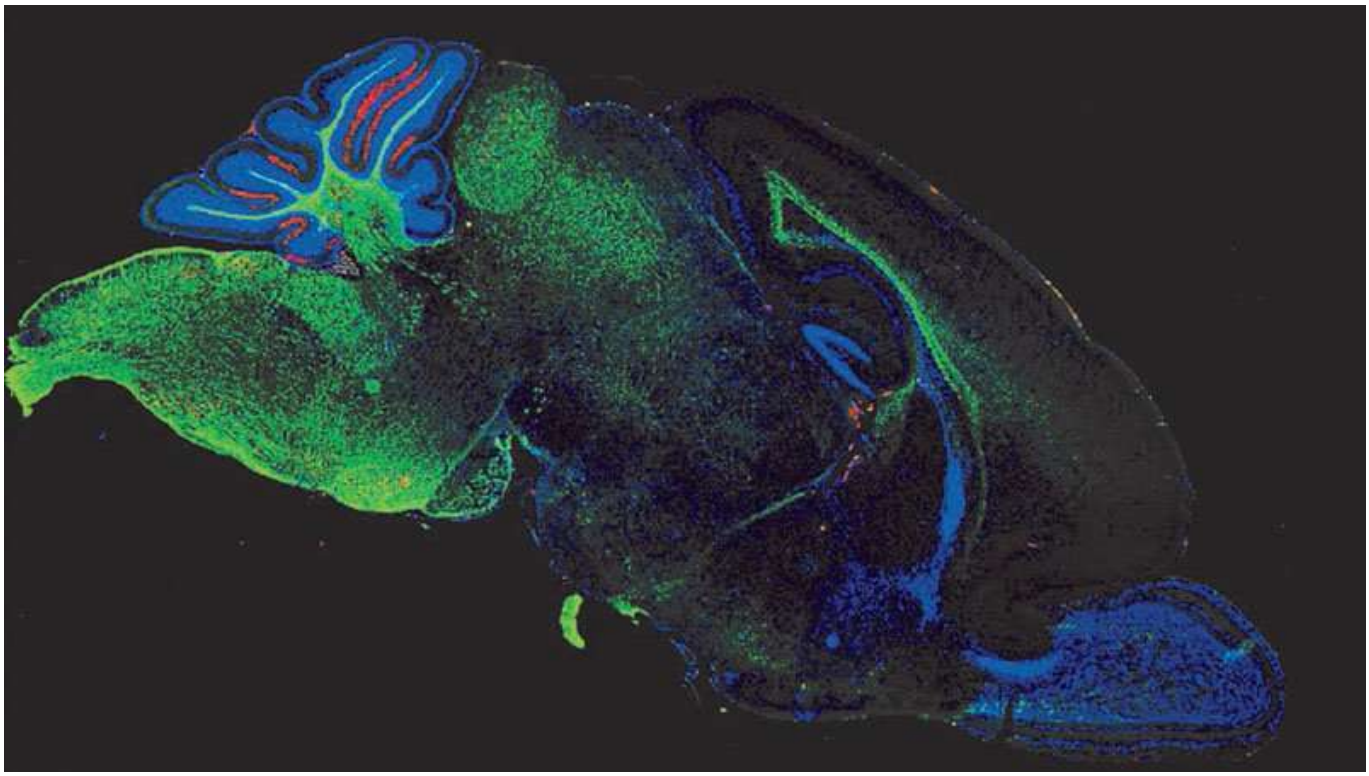
Researchers find the cause of and cure for brain injury associated with gut condition



Representative confocal micrograph showing the expression of myelin basic

protein (MBP – green) and reactive oxygen species (red) in the brain (midsagittal section) of an 11 day old mouse exposed to experimental necrotizing enterocolitis. Credit: David Hackam

Using a mouse model of necrotizing enterocolitis (NEC)—a potentially fatal condition that causes a premature infant's gut to suddenly die—researchers at Johns Hopkins say they have uncovered the molecular causes of the condition and its associated brain injury. The discovery enabled the team to combine efforts with colleagues studying brain inflammation and to identify potential drugs that reverse the brain injury in mice.

Details about the study and findings appear in this week's *Science Translational Medicine*.

"Up until recently, there was no clear understanding of what causes NEC, and the only approach in severe cases was to surgically remove the dead gut from the infant," says David Hackam, M.D., Ph.D., the Garrett Professor and Chief of Pediatric Surgery, a professor of surgery, pediatrics and cell biology at the Johns Hopkins University School of Medicine. "However, NEC survivors have ongoing problems, including significant cognitive impairment."

While the exact causes of NEC in newborns were unclear, the disease is known to occur in premature infants who are fed formula and suffer other stressors, such as bacterial infections. So the team developed a mouse model of NEC by separating newborn mice from their mothers and feeding them formula, subjecting them to a low oxygen chamber twice a day for four days as a stressor and making sure they had similar gut bacteria by feeding them stool from a child who had developed severe NEC. According to Hackam, not only did these mice develop NEC, their brains also showed the same injury as seen in humans and impaired brain function when older. At this point, they were ready to figure out what was causing NEC-associated brain injury in these mice.

First, they looked at whether the immune cells of the brain, so-called microglia, were activated in these NEC mice, which would signify some sort of inflammation. Indeed, the microglia were activated. Others had shown that a protein called TLR4, which binds to bacteria in the gut, is also able to activate microglia in the brain. So they genetically engineered mice to not contain TLR4 on the microglia and gave these mice NEC. The researchers found that these mice did not develop NEC-associated brain injury, suggesting that TLR4 is the cause of that injury.

The team then sought to understand what it is about this gut condition that leads to brain injury. Their previous research had revealed that TLR4 protein was also in the gut. According to Hackam, TLR4 is present in the developing fetal gut at high levels. Those levels drop in full-term infants after delivery. Infants born prematurely, however, maintain high levels of TLR4 in their gut. TLR4 in NEC guts cause cells to release another protein, HMGB1. The team engineered mice to lack HMGB1 and then gave them NEC. These mice showed less microglial activation in the brain than nonengineered mice with

NEC, implying that, indeed, the HMGB1 generated by TLR4 in an inflamed gut is the cause of NEC-associated brain injury.

The work originated through a chance conversation. “One of the cool things about Johns Hopkins is that it’s full of smart people studying all kinds of things. One of the first people I met when I came here in 2014 was Sujatha Kannan, who was studying brain injury in rabbits and had recently shown that an anti-inflammatory applied to the brain of rabbits could prevent cerebral palsy,” says Hackam. So, Hackam and Kannan teamed up to see if this would work in NEC mice. They fed nanoparticles containing antioxidants and tagged with a fluorescent molecule to mice with NEC and examined mouse brains to see where the glowing molecules accumulated.

Sure enough, the brains glowed in the same brain regions where activated microglia are found. Additionally, these brains contained fewer activated microglia, suggesting that the nanoparticle drugs could protect the brain from NEC-associated brain injury.

“We really had to change our thinking from NEC being not only a gut condition to really being a gut-brain condition,” says Hackam. “While this condition manifests more immediately in the gut, neonatologists should also focus on a brain-protective strategy, which could include surgery sooner, gut rest and antibiotics.

“This is a devastating disease, but now that we more clearly understand the molecular underpinnings,” says Hackam, “we are eager to see if it holds true in other models and in patients, so that we have a real chance at ultimately doing better for these babies and their parents,”

Explore further:
Classifying brain microglia: Which are good and which are bad?

More information:
D.F. Nino el al., “Cognitive impairments induced by necrotizing enterocolitis can be prevented by inhibiting microglia activation in mouse brain,” *Science Translational Medicine* (2018). stm.sciencemag.org/lookup/doi/ … scitranslmed.aan0237

Journal reference:
Science Translational Medicine

Provided by:
Johns Hopkins University School of Medicine

Study identifies specific neurological changes related to traumatic brain injury

Traumatic brain injury, or TBI, is often referred to as the “invisible injury” – while on the surface everything seems normal with brain structure, symptoms may present themselves in the behavior of the injured and cannot be explained.

A team from Illinois Institute of Technology, the RDECOM Research Laboratory, the Army’s corporate research laboratory (ARL) and Argonne National Laboratory today released a study that takes a first step to identify the changes that occur in otherwise normal looking brain neurons, with the specific impact forces experienced during head trauma.

According to the Centers for Disease Control and Prevention, about 2.8 million TBI-related emergency department (ED) visits, hospitalizations and deaths occurred in the United States in 2013 alone. Every day, 153 people in the United States die from injuries that include TBI.

This first-of-its-kind study used x-ray diffraction to examine the changes to myelin, the fatty material that wraps around nerve cell projections in the brain and other parts of the body. The study looked at the optic nerves of rats that experienced a range of forces. Starting with no force and working upwards, researchers detected the exact force at which a change in the myelin structure occurred. The changes were tiny, less than a nanometer (a billionth of a meter) but they consistently occur at the same small load of force. What is more, the researchers were able to measure just how much the myelin sheath changed – reflecting the kind of change that occurs in head trauma.

As a result of this work, researchers have a better understanding of what kind of experience, or injury, leads to what kind of damage in the myelin – helping to visualize injuries based on the smallest force necessary to cause it. This information may be critical to knowing when someone has an injury after an accident but before symptoms emerge, and helps supports the decision of when and how to treat them.

“Through this research, we’ve been able to detect specific changes that have never been measured before,” said Joseph Orgel, professor of biology and biomedical engineering, Illinois Institute of Technology. “While more research is needed to develop ways to treat these injuries, identifying the crux of the problem – the impacts that specific forces have on the brain – is an important first step in TBI detection, treatment and prevention.”

The project was supported by grants from ARL and National Institute of General Medical Sciences of the National Institutes of Health.

“Our study examines the initial stage of neural damage with a greater

sensitivity than previously possible, allowing for the determination of a robust relationship between force and damage," said Ashley Eidsmore, ARL electrical engineer and TBI researcher. "These findings and developed methods will aid in the future development of prophylactic methods, including improved soldier protection, targeted surgery and medication. ARL's partnership with the Illinois Institute of Technology and Argonne National Laboratory was critical to achieve this advancement in brain injury science."

Research identifies nerve-signaling pathway behind sustained pain after injury

A toddler puts her hand on a hot stove and swiftly withdraws it. Alas, it's too late—the child's finger has sustained a minor burn. To soothe the pain, she puts the burned finger in her mouth.

Withdrawing one's hand to avoid injury and soothing the pain of that injury are two distinct evolutionary responses, but their molecular origins and signaling pathways have eluded scientists thus far.

Now research led by investigators at Harvard Medical School, published Dec. 10 in *Nature*, identifies the nerve-signaling pathway behind the deep, sustained pain that sets in immediately following injury. The findings also shed light on the different pathways that drive reflexive withdrawal to avoid injury and the subsequent pain-coping responses.

Clinical observations of patients with neurological damage together with past research have outlined the distinct brain regions that differentiate between the reflexive withdrawal from a skin prick, for example, and the long-lasting pain arising from tissue injury caused by the pinprick.

The new study, however, is the first one to map out how these responses arise outside the brain.

The findings, based on experiments in mice, put into question the validity of current experimental approaches for assessing the efficacy of candidate pain-relief compounds. Most current methods rely on measuring the initial, reflexive response that serves to avert tissue injury, rather than on measuring the lasting pain that arises from actual tissue damage, the researchers said. As a result, they said, some drug compounds that might have been successful in assuaging the sustained pain—the lasting sensation of pain that immediately follows injury—could have been dismissed as ineffective because they were assessed against the wrong outcome.

"The ongoing opioid crisis has created an acute and pressing need to develop

new pain treatments, and our findings suggest that a more tailored approach to assessing pain response would be to focus on sustained pain response rather than reflexive protective withdrawal," said study senior author Qiufu Ma, professor of neurobiology in the Blavatnik Institute at Harvard Medical School and a researcher at Dana-Farber Cancer Institute.

"All these years, researchers may have been measuring the wrong response," Ma added. "Indeed, our results could explain, at least in part, the poor translation of candidate treatments from preclinical studies into effective pain therapies."

Previous work by Ma and colleagues, as well as others, points to the existence of two sets of peripheral neurons—the nerve cells located outside the brain and spinal cord. One set of peripheral nerve cells send and receive signals exclusively to and from the superficial layers of the skin. As a first-line of defense against external threats, these peripheral nerve cells are geared toward preventing injury by triggering reflexive withdrawal—think pulling your hand after a pinprick or to avoid the hot tip of a flame. Another set of neurons are dispersed throughout the body and thought to drive the lasting pain that sets in after initial injury and induces pain-coping behaviors such as pressing a banged finger or licking a cut in the skin to sooth the damaged area.

Yet the existence of these neurons could not fully explain how the pain signal travels throughout the body and to the brain. So, Ma and colleagues proposed the existence of another critical player in this relay.

The team focused on a set of neurons called Tac1 emanating from the so-called dorsal horn, a cluster of nerves located at the lower end of the spinal cord that transmit signals between the brain and the rest of the body. The precise function of Tac1 had remained poorly understood so Ma and colleagues wanted to know whether and how these neurons were involved in the sensation of sustained pain.

In a series of experiments, the team assessed pain response in two groups of mice—one with intact Tac1 neurons and another with chemically disabled Tac1 neurons.

Mice with inactivated Tac1 neurons had normal withdrawal reflexes when exposed to a painful stimulus. They showed no notable differences in their withdrawal from pricking or exposure to heat and cold. However, when the researchers injected the animals with burn-inducing mustard oil, they did not engage in the typical paw licking that animals perform immediately following injury. By contrast, mice with intact Tac1 neurons engaged in vigorous and prolonged paw licking to assuage the pain.

Similarly, mice with disabled Tac1 neurons showed no pain-coping responses when their hind paws were pinched—something that induces sustained pain in humans. These animals did not engage in any paw licking as a result of the pinch. Such loss of sensitivity to a specific type of pain mimics the loss of sensation seen in people with strokes or tumors in a particular area of the brain's pain-processing center—the thalamus—that renders them incapable of

sensing lasting pain.

These observations confirm that Tac1 neurons are critical for pain-coping behaviors stemming from sustained irritation or injury but that they play no role in reflexive-defensive reactions to external threats.

Next, researchers wanted to know whether Tac1 neurons shared a common connection with another class of neurons, called Trpv1, present throughout the body and already known to drive the sensation of lasting pain induced by injury. Mice that had functional Tac1 but nonfunctioning Trpv1 neurons responded weakly to pinch-induced pain, showing minimal paw licking. The finding suggests that pain-sensing Trvp1 neurons connect to Tac1 neurons in the dorsal horn of the spinal cord to transmit their signals.

“We believe that Tac1 neurons act as a relay station that dispatches pain signals from the tissue, through Trpv1 nerve fibers all the way to the brain,” Ma said.

Taken together, the results of the study affirm the presence of two lines of defense in response to injury, each controlled by separate nerve-signaling pathways. The rapid withdrawal reflex is nature’s first line of defense, an escape attempt designed to avoid injury. By contrast, the secondary, pain coping response helps reduce suffering and avert widespread tissue damage as a result of the injury.

“We believe it’s an evolutionary mechanism conserved across multiple species to maximize survival,” Ma said.

Source:

https://hms.harvard.edu/news/origins-pain