INSIDE VIEW

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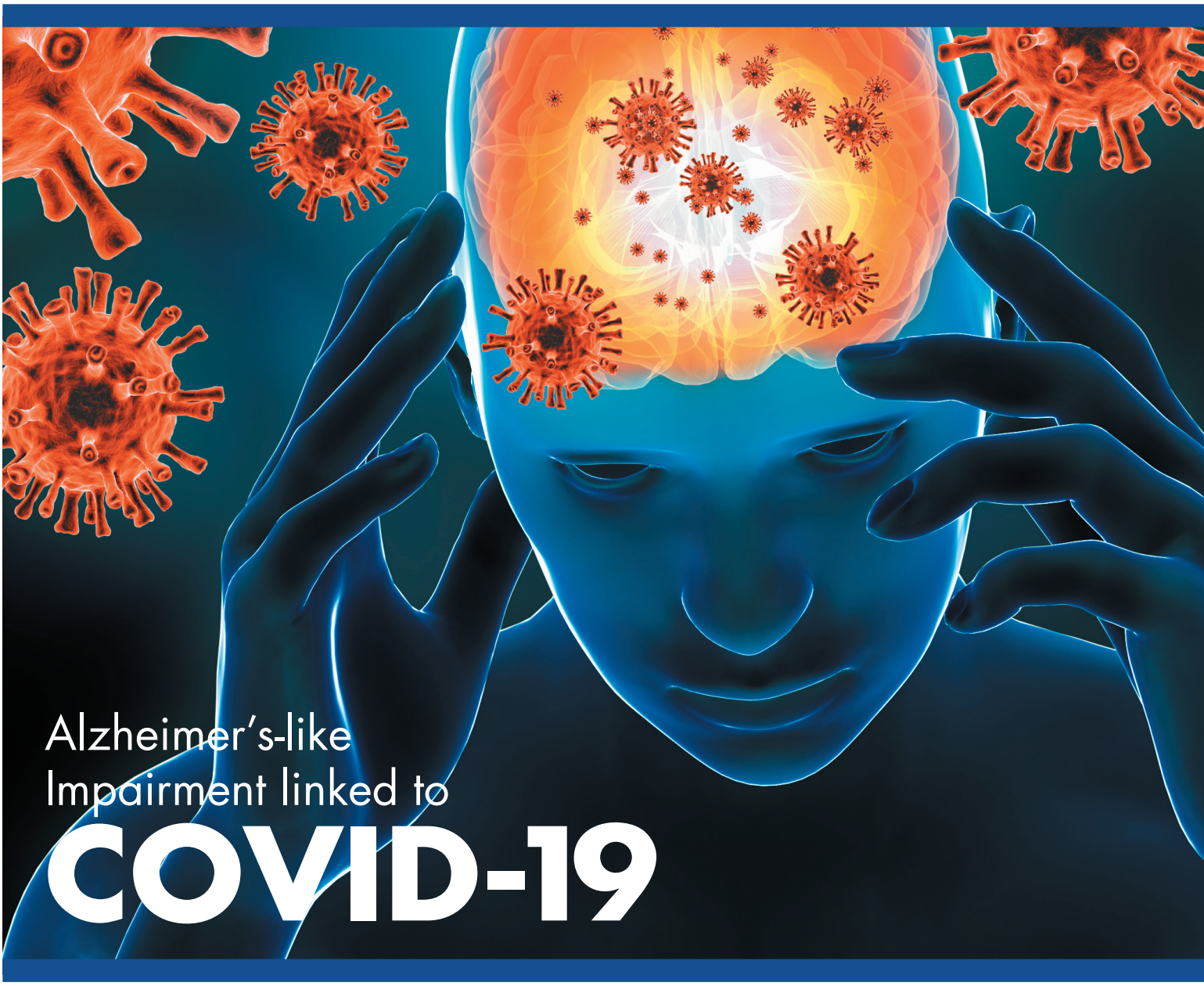

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Sleep Disorders are Associated with Increased Dementia Risk in Patients with TBI

Preliminary results from a study of more than 700,000 patients with traumatic brain injury (TBI) show that those with a sleep disorder had an increased risk of developing dementia.

Results show that over a median follow-up period of more than four years, TBI patients with a diagnosed sleep disorder were 25% more likely to develop dementia. The results were similar when stratified by sex: Having a sleep disorder was associated with a 25.5% increase in the risk of incident dementia in male persons with TBI and a 23.4% increase in the risk of developing dementia in female persons with TBI.

"Our study's novelty is its confirmation of sleep disorders' association with incident dementia in both male and female patients, independently of other known dementia risks," said lead author and primary investigator Dr. Tatyana Mollayeva, an affiliate scientist at the Kite Research Institute, the research arm of the Toronto Rehabilitation Institute and one of the principal research institutes at the University Health Network. Mollayeva is part of the Acquired Brain Injury & Society team at KITE. She is also an assistant professor at the Dalla Lana School of Public Health. "We are also the first to report on the risks that sleep disorders and other factors pose separately for male and female patients with TBI."

The retrospective study involved a province-wide cohort of all adult patients who were free of dementia when admitted to the emergency department or acute care hospital with a diagnosis of TBI between May 2003 and April 2013. The total sample comprised 712,708 patients with TBI of all severities. Their median age was 44 years, and 59% were male.

Over a median follow-up period of 52 months, 32,834 patients – or 4.6% – developed dementia. Analyses controlled for age, sex, income level, injury severity, and known comorbidity risks.

"The strong links to incidence of dementia in both sexes suggest a need for more targeted sleep disorders risk awareness in patients with TBI," said Mollayeva. ■

2021-22 Calendar of Events

Oct

4-5
11th Annual Traumatic Brain Injury Conference
Washington, D.C.
tbiconference.com/home

6-9
Pediatric Acquired Brain Injury Conference
New York, NY
ipbis2021.org

14-15
Brain SoCal Med-Legal Conference 2021
Los Angeles, CA
brainsocal.glueup.com/event/brain-socal-med-legal-conference-2022-20012

14-15
Brain Injury Association of Illinois Conference
Oakbrook Terrace, IL
biail.com/calendar.htm

Nov

5
BIA Colorado Brain Injury Symposium
Lakewood, CO
biacolorado.org/conferences/

Dec

2-3
Intl Conference on Traumatic Brain Injury and Biological Mechanisms
Amsterdam, Netherlands
waset.org/traumatic-brain-injury-and-biological-mechanisms-conference-in-december-2021-in-amsterdam

Mar 2022

30-31
BIA of Massachusetts Annual Conference
Marlborough, MA
biama.org

30-1
American Society for Neuroscience Conference
St. Louis, MO
asnr.com/i4a/pages/index.cfm?pageid=3851

May

13-19
ASNR 2022 Symposium and Annual Meeting
New York, NY
asnr.org/events/upcoming-meetings/asnr/

15-18
2022 IRSG Annual Conference
Baltimore, MD
irsghome.org/

Jun

26-29
Neurotrauma 2022
Atlanta, GA
neurotrauma.org/symposium/2022-atlanta/general-info-2022

Articles are sourced from scientific journals, universities and publications that contribute to the ongoing research of brain injury.

Study Identifies How COVID-19 Linked to Alzheimer's Disease-like Cognitive Impairment

"We discovered that SARS-CoV-2 infection significantly altered Alzheimer's markers implicated in brain inflammation and that certain viral entry factors are highly expressed in cells in the blood-brain barrier."

A new Cleveland Clinic-led study has identified mechanisms by which COVID-19 can lead to Alzheimer's disease-like dementia. The findings, published in Alzheimer's Research & Therapy, indicate an overlap between COVID-19 and brain changes common in Alzheimer's, and may help inform risk management and therapeutic strategies for COVID-19-associated cognitive impairment.

Reports of neurological complications in COVID-19 patients and "long-hauler" patients whose symptoms persist after the infection clears are becoming more common, suggesting that SARS-CoV-2 (the virus that causes COVID-19) may have lasting effects on brain function. However, it is not yet well understood how the virus leads to neurological issues.

"While some studies suggest that SARS-CoV-2 infects brain cells directly, others found no evidence of the virus in the brain," says Feixiong Cheng, Ph.D., assistant staff in Cleveland Clinic's Genomic

Medicine Institute and lead author on the study. "Identifying how COVID-19 and neurological problems are linked will be critical for developing effective preventive and therapeutic strategies to address the surge in neurocognitive impairments that we expect to see in the near future."

In the study, the researchers harnessed artificial intelligence using existing datasets of patients with Alzheimer's and COVID-19. They measured the proximity between SARS-CoV-2 host genes/proteins and those associated with several neurological diseases where closer proximity suggests related or shared disease pathways. The researchers also analyzed the genetic factors that enabled SARS-COV-2 to infect brain tissues and cells.

While researchers found little evidence that the virus targets the brain directly, they discovered close network relationships between the virus and genes/proteins associated with several neurological diseases, most notably Alzheimer's, pointing to pathways by which COVID-19 could lead to AD-like dementia. To explore this further, they investigated potential associations between COVID-19 and neuroinflammation and brain microvascular injury, which are both hallmarks of Alzheimer's.

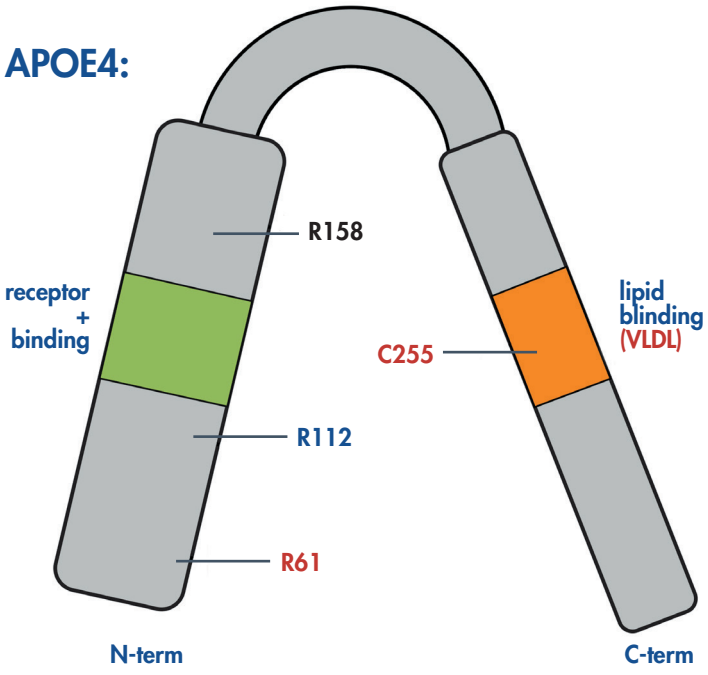
"We discovered that SARS-CoV-2 infection significantly altered Alzheimer's markers implicated in brain inflammation and that certain viral entry factors are highly expressed in cells in the blood-brain barrier," explained Dr. Cheng. "These findings indicate that the virus may impact several genes or pathways involved in neuroinflammation and brain microvascular injury, which could lead to Alzehimer's disease-like cognitive impairment."

The researchers also found that individuals with the allele APOE E4/E4, the greatest genetic risk factor for Alzheimer's, had decreased expression of antiviral defense genes, which could make these patients more susceptible to COVID-19.

"Ultimately, we hope to have paved the way for research that leads to testable and measurable biomarkers that can identify patients at the highest risk for neurological complications with COVID-19," said Dr. Cheng.

Dr. Cheng and his team are now working to identify actionable biomarkers and new therapeutic targets for COVID-19-associated neurological issues in COVID long-haulers using cutting-edge network medicine and artificial intelligence technologies. ■

"Ultimately, we hope to have paved the way for research that leads to testable and measurable biomarkers that can identify patients at the highest risk for neurological complications with COVID-19"



Novel Interactions Between Proteins That Help in Recovering from Brain Injury

Results from experiments revealed that an increase in the number of hevin-calcyon interactions in the brain could promote synaptic contacts and reorganization, which could help in the early recovery of the impaired brain.

Patients with brain injury (caused by stroke or trauma) primarily rely on rehabilitation therapy for recovery, as there are no other known effective treatment methods. The rate of recovery from brain injury observed in adults is significantly slower (or the recovery is impossible) than that observed in young children. The consensus among researchers is that the number of excess neural stem cells capable of restoring brain functions is lower in a mature brain than that in the brain of young children.

A Korean research team reported a novel mechanism to describe the brain injury recovery process. The researchers reported that when the animal model experiment was conducted, the time taken to recover from a brain injury could be controlled by regulating the proteins. The Korea Institute of Science and Technology (KIST) has released an announcement that a team led by Dr. Eun Mi Hwang of the Brain Science Institute, KIST collaborated with another team led by Prof. Kyoungho Suk of the School of Medicine, Kyungpook National University and reported the presence of a novel interaction between proteins (hevin-calcyon); this interaction plays a critical role in the brain injury recovery process in adults. The researchers also revealed that this interaction plays an important role in the early stages of recovery.

The researchers working at KIST identified the calcyon protein as a novel interaction partner of hevin, a protein secreted by the glial cells present in the brain. They also reported that the interaction between the proteins played a critical role in the recovery process of neuronal cells present in an injured adult brain. As neurons are cells that directly influence brain activity, it is believed that brain diseases can be cured when they are recovered and/or treated.

*Glial cells: Cells that support the tissues of the central nervous system, provide nutrients to neurons inside the brain and spinal cord, and create a chemical environment suitable for the activities of neurons

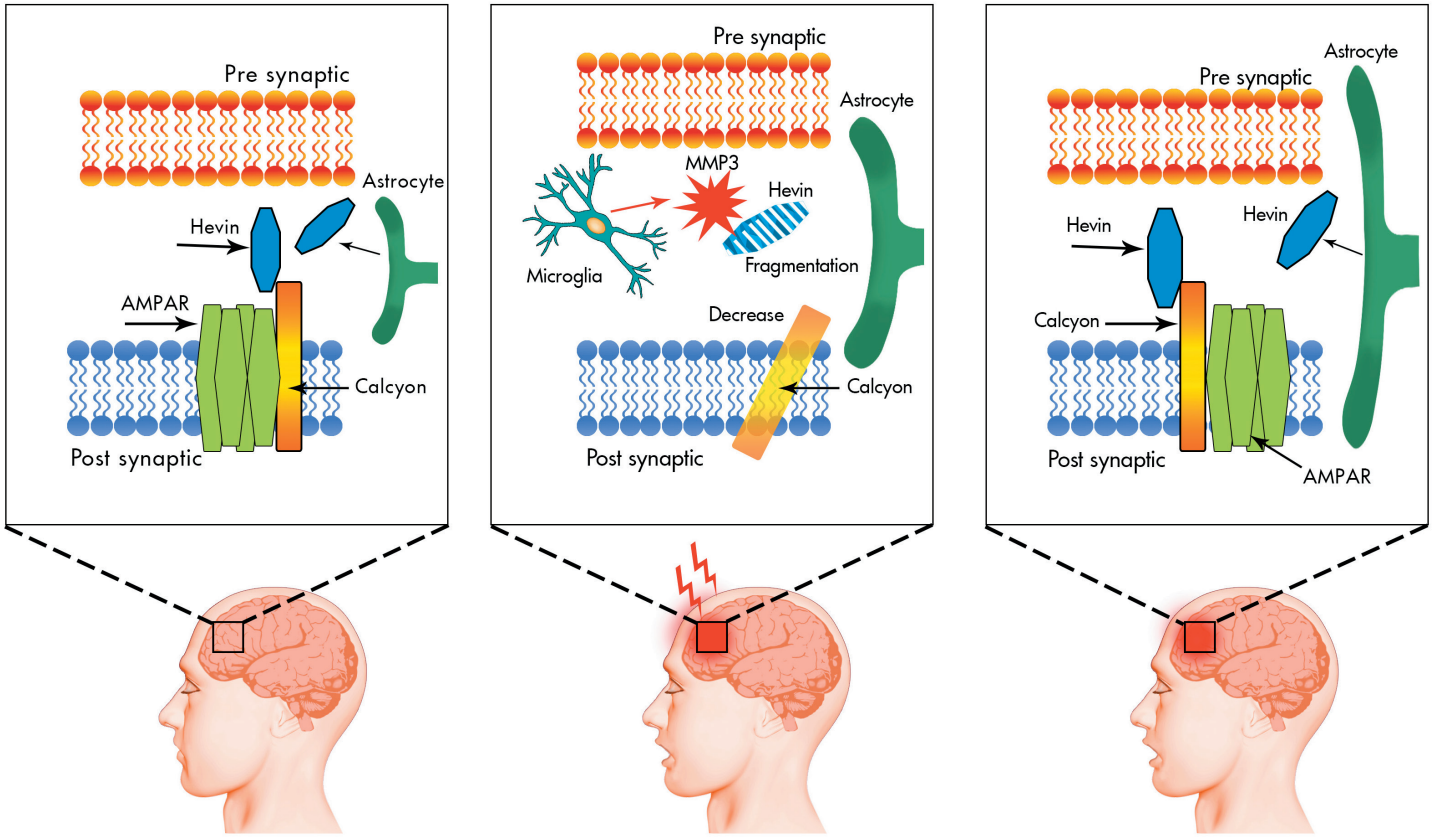
The results from the experiments revealed that an increase in the number of hevin-calcyon interactions in the brain could promote synaptic contacts and reorganization, which could help in the early recovery of the impaired brain. The hevin-calcyon interaction and the expression of these proteins were confirmed by studying healthy

brain tissues. It was also observed that the number of interactions in patients suffering from the condition of traumatic brain injury was significantly reduced.

Researchers at the Kyungpook National University studied the recovery process of brain injury by studying the hevin and calcyon interaction using a brain injury animal model. They reported that the neuroinflammatory response-induced proteases formed in the early stages of brain injury resulted in the fragmentation of hevin. This also impeded the generation of the hevin and calcyon interaction. Experiments were conducted using an animal model of brain injury. It was observed that the recovery time could be reduced to approximately 2 to 3 weeks (from 4 weeks) if an inflammatory response inhibitor was administered directly to the injured region of the brain. The rate of recovery could be further slowed by administering an additional inflammatory protein.

The joint research team reported that the absence of the hevin-calcyon interaction in the early stages (a critical period in the recovery process of brain injury) of the recovery process might negatively impact the effective recovery process. The reported result is the outcome of the five years of persistent efforts by the team led by Dr. Eun Mi Hwang of KIST (this team identified the novel interaction between proteins), team led by Dr. Hoon Ryu of KIST (this team investigated human traumatic brain injury), and team led by Prof. Kyoungho Suk of the Kyungpook National University (this team studied the properties of inflammation using various animal models). Each team contributed to the findings based on their area of expertise.

Dr. Eun Mi Hwang of KIST said, "The hevin-calcyon interaction can potentially help in treating brain diseases as brain injury and neurodegenerative diseases can result in the generation of inflammatory responses." She also added, "The findings can potentially help in the development of procedures for treating refractory brain diseases caused by impaired synaptogenic activity." ■



Normal Condition Pathological Condition Recovery Condition

Strict Rest After Sports-related Concussion Slows Recovery and May Prolong Symptoms

Recent research shows that progressive moderate aerobic exercise within the first week helps aid recovery.

Strict rest after a sports related concussion slows recovery and may prolong symptoms, says a consensus statement drawn up by a US expert panel on how best to treat and manage the condition, and published in the British Journal of Sports Medicine.

Most of these concussions get better within a month and can be effectively treated, it says.

Persisting symptoms are thought to be a complex interplay between the physical and psychological effects of the new injury and underlying conditions.

The consensus statement was developed by the Team Physician Consensus Conference (TPCC), an annual project-based alliance of six major professional associations, with the aim of helping team doctors to provide the best medical care for athletes.

It updates a previous version on the management of concussion, published in 2011.

Data harvested from US emergency department visits, doctors' appointments, and a high school injury surveillance system (RIO) estimate the number of sports related concussions to be between 1 and 1.8 million every year in the USA alone among those up to the age of 18, with around 400,000 occurring in high school athletes.

But the symptoms of concussion aren't specific and there are currently no clinically useful diagnostic tests, such as blood tests, genetic tests or standard imaging techniques. So, the true incidence and prevalence of sports related concussion remain unknown, says the statement.

Signs and symptoms indicating more severe brain or neck (cervical spine) injury and warranting immediate emergency care include:

- Immediate seizure (at or minutes after impact)
- More than brief loss of consciousness
- Severe or worsening headache
- Persistent or recurrent vomiting
- Increasing lethargy, confusion
- Tingling or numbness in hands and/or feet; double vision
- Neck pain; bony tenderness; limited range of movement and/or deformity

And there is a range of symptoms that may occur immediately or some-time later, which may also be indicative of concussion, says the statement.

These include: amnesia; disorientation; brain fog; inability to focus; slurred speech; excessive drowsiness; headache; dizziness; balance issues; visual disturbances; hypersensitivity to noise; irritability; and sleep disturbances.

Most sports related concussion is treatable, says the statement. And most affected athletes

will recover fully within 2 (adults) to 4 weeks (children).

The number and severity of the initial array of symptoms best predict how long it will take to recover.

Factors that may prolong or complicate recovery include: previous concussions; loss of consciousness for more than 1 minute; younger age; pre-existing conditions, including migraine, ADHD, learning disabilities, depression, anxiety/panic attacks, and motion sickness.

Current evidence suggests that strict rest after a concussion slows recovery and increases the probability of prolonged symptoms. Recent research shows that progressive moderate aerobic exercise within the first week helps aid recovery.

Most athletes don't require over-the-counter and/or prescription meds for acute symptoms. And there's no current evidence to suggest that 'nutraceuticals' help to either ward off or treat concussion, says the statement.

Persisting symptoms, such as fatigue, headache, and anxiety, aren't usually caused by one factor alone, but are thought to be a complex interplay between the physical and psychological effects of the new injury and underlying conditions, says the statement.

In these circumstances, treatment should focus on the particular symptom: cognitive behavioral therapy and/or lifestyle changes to sleep, nutrition, and hydration, for example.

More high-quality research is needed to fully understand young people's risks of taking part in sport after concussion and the effects on their long-term brain health and wellbeing, says the statement.

"Most athletes who have been concussed will get better, and will be able to return to play," comments Dr Margot Putukian, TPCC executive committee member.

"Each injury is unique and will have its own timeline. But athletes should take comfort in knowing that there are treatments out there, and there are steps they can take to aid their own recovery," she adds. ■

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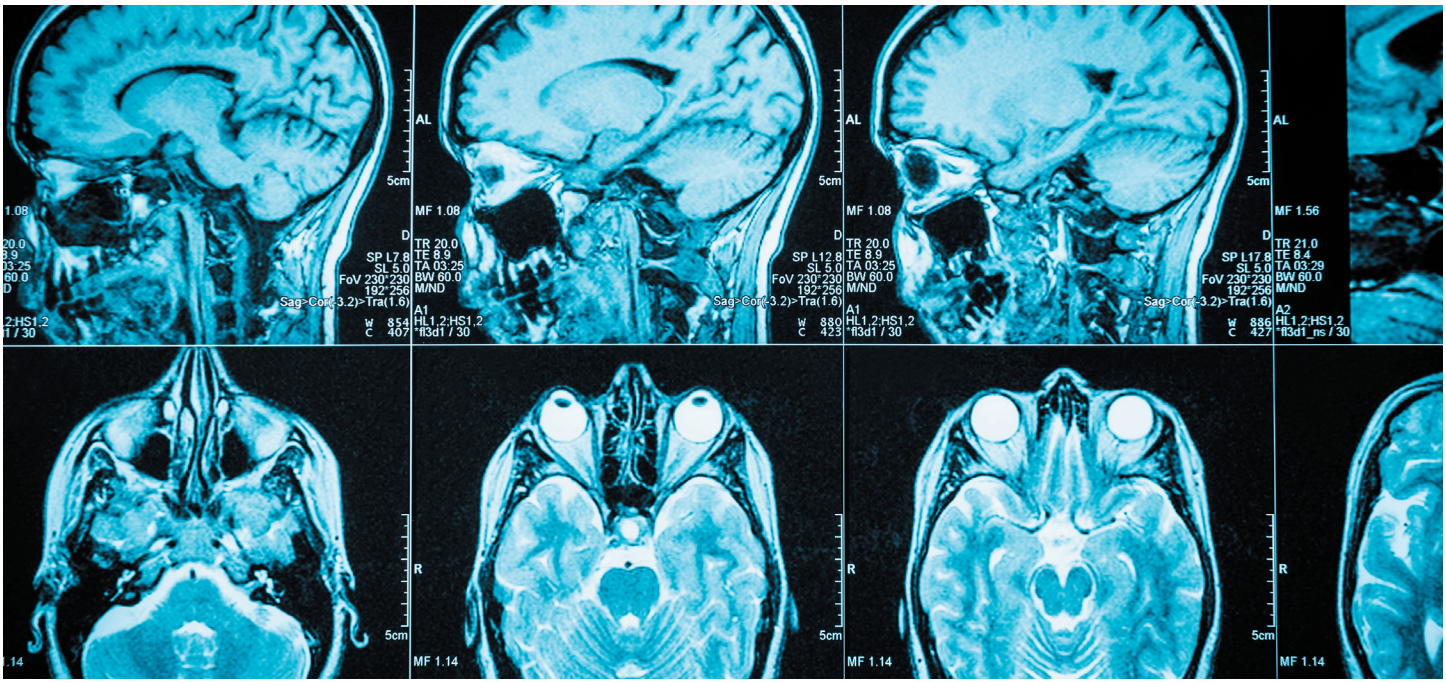


New Drug to Halt Dementia After Multiple Head Injuries

New research findings could halt the progression of chronic traumatic encephalopathy (CTE) in sports people who sustain repeated blows to the head.

A world-first international study led by the University of South Australia has identified a new drug to stop athletes developing dementia after sustaining repeated head injuries in their career.

The link between concussion and neurogenerative diseases is well established, but new research findings could halt the progression of chronic traumatic encephalopathy (CTE) in sports people who sustain repeated blows to the head.

CTE is a progressive and fatal brain disease associated with the accumulation of a protein known as hyperphosphorylated tau which affects cognition and behavior.

In a paper published in Scientific Reports, UniSA Emeritus Professor Bob Vink and colleagues show how repeated concussions can cause CTE and a way to block it with a specially developed drug.

The findings will potentially have significant implications for athletes who play contact sports - such as boxers and footballers

- as well as military veterans sustaining head injuries in conflict.

The team of researchers from Adelaide, Melbourne and the United States say the brain releases a neurotransmitter called substance P in the event of a head injury, causing abnormal amounts of the tau protein to collect inside neurons.

"Tau protein tangles are a feature of CTE, which reportedly leads to memory problems, confusion, personality changes, aggression, depression and suicidal thinking," Prof Vink says.

"Our research shows that by blocking substance P with a specific drug, we can prevent the tau protein tangles from developing in the brain and causing neurological problems."

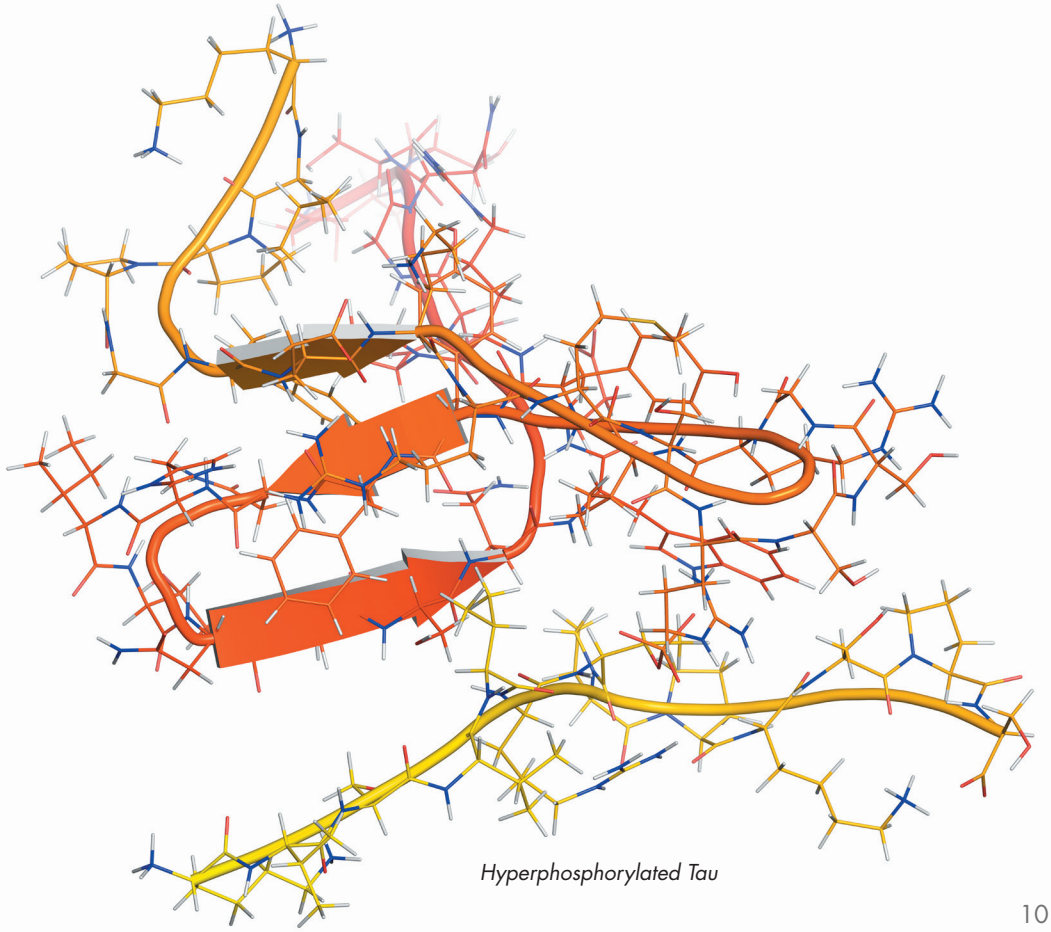
The treatment was successfully tested in animal models, giving hope that CTE can be prevented in humans.

Prof Vink says the next step is human clinical trials, but that could take several years given that currently CTE can only be diagnosed post-mortem.

A study of 14,000 Americans over 25 years, published in Alzheimer's and Dementia in March, showed that people who sustained even one head injury were 25 per cent more likely to develop dementia later in life. This risk increased with multiple traumatic brain injuries.

The Guardian also recently reported that an analysis of late AFLW player Jacinta Barclay's brain uncovered neurological damage at age 29, highlighting the risks of repeated concussions to both sexes. Previous research has focused on the impact of brain injuries in male athletes, but females are more likely to sustain concussions. ■

"Tau protein tangles are a feature of CTE, which reportedly leads to memory problems, confusion, personality changes, aggression, depression and suicidal thinking"



Hyperphosphorylated Tau

History of Traumatic Brain Injury Linked to Higher Rates of Prescription Opioid Use and Misuse

"Persons with TBI compared to those without had over 52% increased risk for using prescription opioids in the past year, and over 65% increased risk for prescription opioid misuse."

Adults with a history of traumatic brain injury (TBI), even years previously, are at increased risk of use and misuse of prescription opioid medications, reports a study in a recent special issue of the Journal of Head Trauma Rehabilitation (JHTR). The official journal of the Brain Injury Association of America.

After adjustment for other factors, "Persons with TBI compared to those without had over 52 percent increased risk for using prescription opioids in the past year, and over 65 percent increased risk for prescription opioid misuse," according to the report by Rachel Sayko Adams, PhD, MPH, of Brandeis University, Waltham, Mass. The JHTR special issue presents eight invited research papers providing evidence for the hypothesis linking a history of TBI to a unique pattern of increased vulnerability to pain and other interrelated risks for opioid use and its potential consequences, including overdose.

New data support 'Perfect Storm' hypothesis of opioid risks after TBI

The study included data on nearly 3,500 participants from a 2018 study of health risks among adults in Ohio. Overall 22.8 percent of participants said they had at least one TBI sometime in their lives. Of these individuals, more than two-thirds had had a TBI with loss of consciousness, most before age 20.

One-fourth of participants (25.5 percent) reported using a prescription opioid in the past year. About three percent met criteria for prescription opioid misuse – defined as using opioids more frequently or in higher doses than prescribed and/or using a prescription opioid not prescribed to the respondent. (The study did not address use of illicit opioids, such as heroin, following TBI – a gap in knowledge requiring further research.)

Participants with a history of TBI were more likely to report prescription opioid use in the past

year: 30.9 percent, compared to 23.9 percent of those without a TBI history. After controlling for demographic factors (sex, age, race/ethnicity, and marital status), history of TBI was associated with a 52 percent increase in the odds of prescription opioid use and a 65 percent increase in the odds of prescription opioid misuse.

The findings support the hypothesis – outlined by Dr. Adams and other TBI researchers, in a paper published last year – that persons with a history of TBI face a three-phase "Perfect Storm" of increased opioid risks:

- Phase I: Greater exposure to opioids related to pain and other factors following TBI
- Phase II: Greater likelihood of progression to long-term opioid treatment, opioid misuse, or diagnosed opioid use disorder (OUD)
- Phase III: Greater barriers to successful treatment for patients with TBI who develop OUD.

These "cascading vulnerabilities" may combine to lead to potential consequences of opioid misuse and OUD, including increased risk for overdose and suicide.

The special issue papers add to the growing body of evidence that persons with a history of TBI are more likely to be treated with prescription opioids (Phase I), in both civilian and military settings. Some papers provide new evidence that a history of TBI is associated with increased odds of opioid misuse (Phase II), in adolescents as well as adults. So far, there have been few studies investigating if TBI leads to increased obstacles to OUD treatment (Phase III).

Persons with TBI are at increased risk for pain, which is thought to be an important driver of their increased opioid risks. One of the new studies finds that opioids are more likely to be prescribed for patients with comorbid pain and/or psychological health conditions after TBI. Previous research has found that alcohol or drug use is a risk factor for TBI, and persons with TBI are at elevated risk for substance use after injury. The new studies in the special issue suggest that prescription opioid use follows a similar cyclical pattern with TBI as alcohol or other drugs.

"Empirical investigation into each element of the 'perfect storm' is needed to identify treatment targets and prevention opportunities," Dr. Adams writes in an introduction to the special issue. She and her colleagues believe that substance use treatment providers need to be trained to screen for and address problems related to a history of TBI, while rehabilitation professionals treating TBI patients should perform screening for at-risk substance use. ■

High Risk of Divorce After TBI? Not Necessarily

Traumatic brain injury (TBI) has a major impact on the lives of affected patients and families. But it doesn't necessarily lead to an increased risk of marital instability, as two-thirds of patients with TBI are still married to the same partner 10 years after their injury, reports a study in a recent issue of the Journal of Head Trauma Rehabilitation (JHTR). The official journal of the Brain Injury Association of America.

For marriages that do end, divorce most often occurs within the first year after TBI, according to the new research by Flora M. Hammond, MD, of Indiana University School of Medicine, Indianapolis, and colleagues. "Our data dispel myths about risk of divorce after TBI and suggest a message of hope," the researchers write.

Findings may help in assessing risk and targeting timing marital interventions after TBI

Dr. Hammond and colleagues analyzed long-term follow-up data on 1,423 patients with TBI, all of whom were married at the time of their injury. Patients were drawn from the Traumatic Brain Injury Model Systems (TBIMS) database enrolling persons hospitalized with TBI. Average age at the time of injury was 44 years; about three-fourths of patients were men.

Ten years after TBI, 66 percent of patients with TBI remained married to the same person, without separation or divorce. Of marriages that ended, 68 percent did so within five years after TBI, including 39 percent within the first year.

The study also looked at factors associated with a higher or lower risk of divorce or separation. "Marital stability over the 10-year period was higher for those who were older, were female, and had no problematic substance use history," the researchers write. The risk of a breakup didn't seem to be related to race/ethnicity, education, cause of injury, or injury severity.

Marital stability has a major impact on the ability to resume normal life and functioning in persons with TBI. Some reports have suggested high divorce rates after TBI. However, in previous studies, reported rates of marital instability after TBI varied widely: from 22 to 85 percent. Long-term follow-up in a large sample of patients with TBI are major strengths of the new study.

The results question previous studies suggesting a high divorce rate among patients who are married at the time they sustain a TBI. The study also provides insights into risk factors for a marital breakup after TBI. The findings are consistent with the known bidirectional link between TBI and substance use. "While substance use itself may not cause marital instability, a spouse's perception that substance use is problematic may contribute to marital instability," Dr. Hammond and coauthors write.

The high risk of marital loss within the first few years after TBI suggests that early education and support might be helpful. The researchers note some important limitations of their study – including the lack of information on the quality of the marital relationship before TBI.

The findings may help to identify couples who may be at high risk of marital instability after TBI, and to guide patient and family education, relationship counseling, and other marital interventions, Dr. Hammond and colleagues believe. They conclude, "Interventions aimed at substance use prevention and functional improvement may also have relevance to facilitating marital stability." ■

Two-thirds of patients with TBI are still married to the same partner 10 years after their injury.

Young Athletes with History of Concussions May Have More Changes to Their Brains

A new study suggests athletes with a history of concussion may show more brain injury from a later concussion, particularly in middle regions of the brain that are more susceptible to damage, when compared to athletes with no history of concussion. The research is published in the online issue of Neurology®, the medical journal of the American Academy of Neurology. The athletes participated in sports like football, volleyball and soccer.

"We know concussions may have long-term effects on the brain that last beyond getting a doctor's clearance to return to play," said study author Tom A. Schweizer, PhD, of St. Michael's Hospital in Toronto, Canada. "It is unclear, however, to what extent the effects of repeated concussion can be detected among young, otherwise healthy adults. We found even though there was no difference in symptoms or the amount of recovery time, athletes with a history of concussion showed subtle and chronic changes in their brains."

This study focused on changes within two areas in the middle of the brain that are especially vulnerable to concussion. Researchers focused on blood flow in the cingulate cortex and white matter microstructure in the corpus callosum. Changes in blood flow and microstructure that show up on brain scans can indicate underlying brain injury. The cingulate cortex is a layer of gray matter that coordinates sensory and motor skills. Below it is the corpus callosum, a broad band of nerve fibers linking the two hemispheres of the brain.

The study looked at 228 athletes with an average age of 20. This included 61 with a recent concussion and 167 without. Within the first group, 36 had a history of concussion. Within the second group, 73 had a history of concussion.

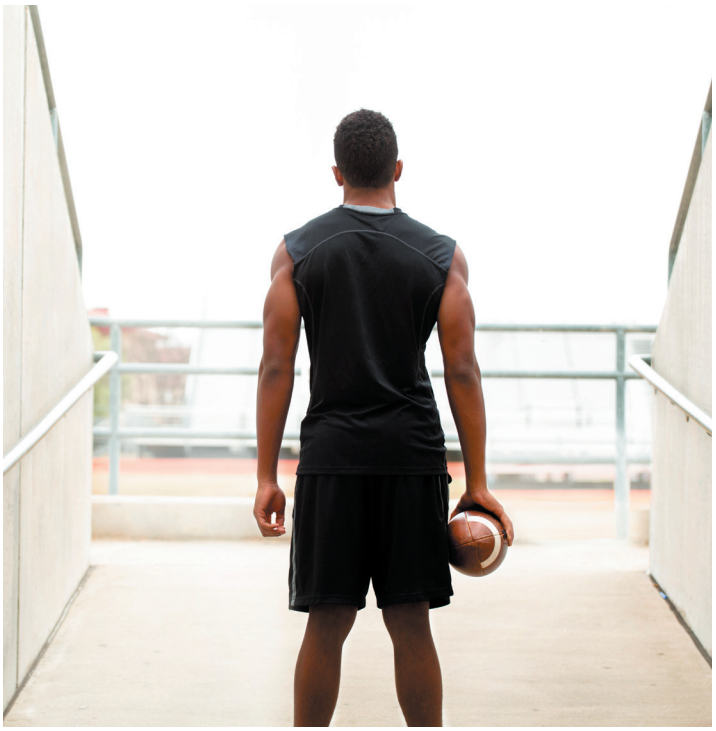
Researchers took up to five brain scans of each recently concussed athlete, from time of injury to one year after returning to play.

Researchers found that one year after a recent concussion, athletes with a history of concussion had sharper declines in blood flow within one area of the cingulate compared to those without a history of concussions. Those with a history of concussion had an average cerebral blood flow of 40 milliliters (mL) per minute, per 100 grams (g) of brain tissue. Those without a history of concussion had an average cerebral blood flow of 53 mL per minute, per 100g of brain tissue.

In athletes with a history of concussion, in the weeks after a new concussion, researchers also found microstructural changes in a region of the brain called the splenium, which is part of the corpus callosum.

"Our findings suggest that an athlete with a history of concussion should be watched closely, as these subtle brain changes may be worsened by repeated injury," said Schweizer. "Additionally, our results should raise concern about the cumulative effects of repeated head injuries later in life."

A limitation of the study is that athletes reported their own histories of concussion and could be inaccurate. Further research is needed that would follow athletes over time. ■



Altered Functional Brain Network Connectivity Associated with Symptoms of Post-traumatic Stress in COVID-19 Survivors

Some COVID-19 survivors experience long-term mental health problems, including anxiety, depression and post-traumatic stress disorder.

Although COVID-19 is primarily considered a respiratory disease, experts recognize it also affects the nervous system, sometimes causing severe neurological symptoms. Some COVID-19 survivors also experience long-term mental health problems, including anxiety, depression and post-traumatic stress disorder.

Few studies have examined functional abnormalities in the brain, which might reveal the physiological processes that underlie prolonged mental

health symptoms in COVID-19 survivors.

In this paper, published in Neurobiology of Stress, the researchers set out to determine whether survivors experience functional disruption of large-scale brain networks, collections of discrete and widespread regions of the brain that work together to perform complex cognitive tasks. They collected functional MRI (fMRI) data and self-reported post-traumatic stress symptoms from 50 COVID-19 survivors, along with matched control subjects. The COVID-19 survivors were discharged between February and March 2020 from hospitals in Wuhan, China, and were tested about six months after their discharge.

The findings showed COVID-19 survivors self-reported significantly more symptoms of post-traumatic stress than the controls. The study also revealed COVID-19 survivors exhibited abnormal patterns of brain connectivity over time, which were significantly associated with greater post-traumatic stress symptoms.

"Until recently," said Calhoun, a Georgia Research Alliance Eminent Scholar, "analysis approaches used for fMRI data assumed that the brain's functional connectivity was static. But we now have approaches that can capture dynamic functional brain connectivity, showing the way brain patterns change over time in fundamental and reoccurring ways."

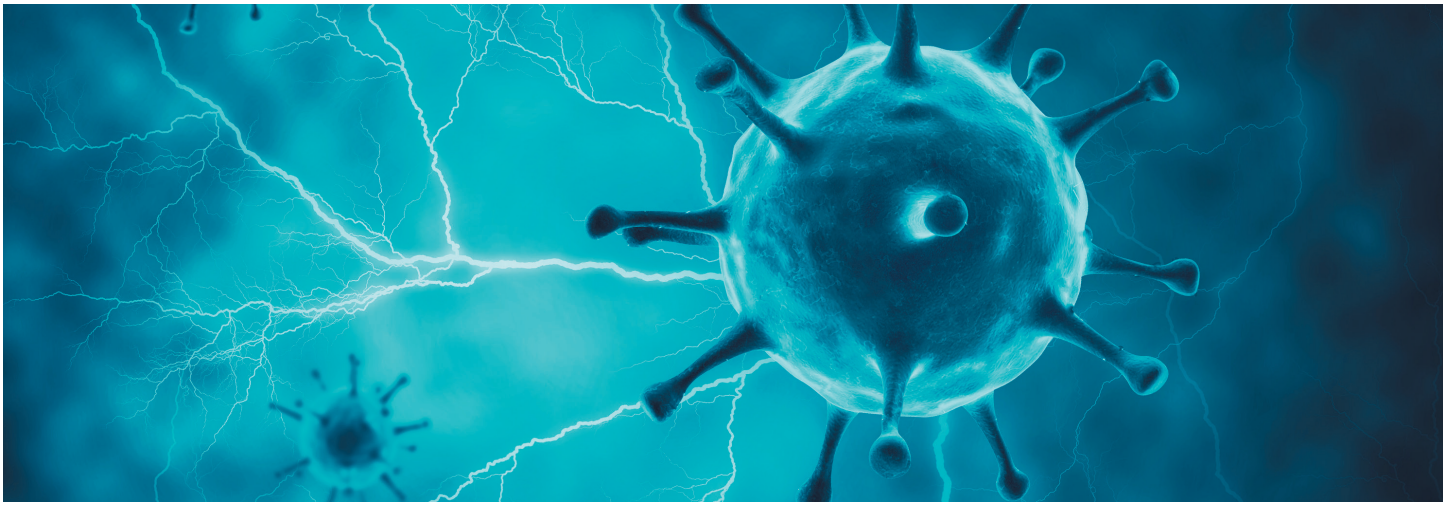
The researchers identified three distinct, reoccurring states of functional connectivity in the subjects' brains. The COVID-19 survivors showed an increased occurrence of a particular state marked by patterns of connections between brain networks involving sensorimotor functions and visual networks.

"When we looked within the COVID-19 survivor group, we also found a significant relationship between the severity of their post-traumatic stress symptoms and how often their brain patterns are in that state," said Calhoun. "If they spend more time in that state, they tend to have higher values on those symptom scales."

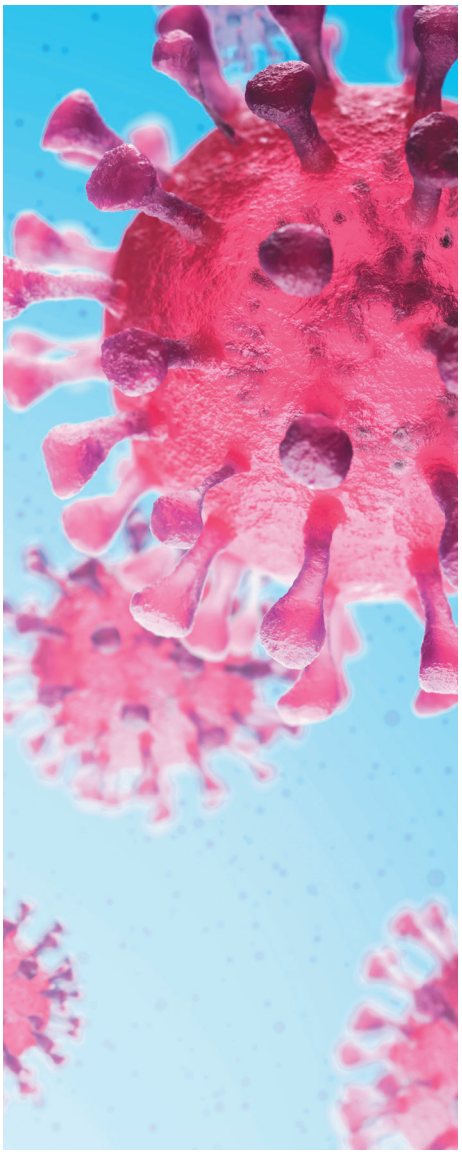
"Our findings provide evidence that COVID might affect transient brain dynamics rather than its ongoing activity," said Zening Fu, the study's first author and a research scientist at TReNDS.

The results highlight the importance of evaluating transient, time-varying functional network changes among COVID-19 survivors, although Calhoun notes there are still many unanswered questions, including why this one brain state is linked to post-traumatic stress. The research team is also interested in replicating the study using other data and looking at changes within subjects before and after contracting COVID-19. ■

"Our findings provide evidence that COVID might affect transient brain dynamics rather than its ongoing activity."



Covid Can Infect Brain Cells



The coronavirus can infect brain cells, leading to a reaction that could possibly trigger neurological and psychological complaints, Dutch researchers said on Thursday.

Although the spread of coronavirus rapidly stops, leading to limited damage after entering the brain via the nose, it triggers cytokines, small proteins that act as messengers within the immune system, said the study published in the US-based mSphere microbiology journal.

"These can play a role in local infections… that possibly contribute to neurological and psychological complaints among many (ex) patients," said the study, done by the Erasmus University Medical Centre in Rotterdam.

"What we saw was similar to the fact that infection by SARS-CoV-2 seldom leads to serious encephalitis in which the virus spreads uncontrollably through the brain," said Debby van Riel, virologist at Erasmus University.

"But the fact that SARS-CoV-2 possibly can enter the brain via the olfactory nerve and locally infect cells, which leads to an inflammatory response, can certainly contribute to neurological disorders," she said in a statement.

Since the coronavirus pandemic started, patients around the world have reported neurological and psychiatric disorders such as memory problems, headaches, rare psychoses and in some cases encephalitis.

One in three people who contracted COVID were diagnosed with these disorders within six months of being infected, said a large study recently published in The Lancet Psychiatry specialist journal.

Growing data has indicated that the virus could enter the brain via the olfactory nerve, the Erasmus study added.

However, what happens when the virus entered the brain remained poorly understood, it said.

"Apart from our findings, the immune system probably also plays a role," said Femke de Vrij of Erasmus' psychiatry department.

"More research is needed," she added.

"We have now observed the virus in cells over a short period of time. We also just looked at a limited number of brain cells," said De Vrij, adding that further research "will tell us more about what the viral infection does with brain structures over the short and longer term." ■

One in three people who contracted COVID were diagnosed with memory problems, headaches, rare psychoses, and in some cases encephalitisdis within six months of being infected.

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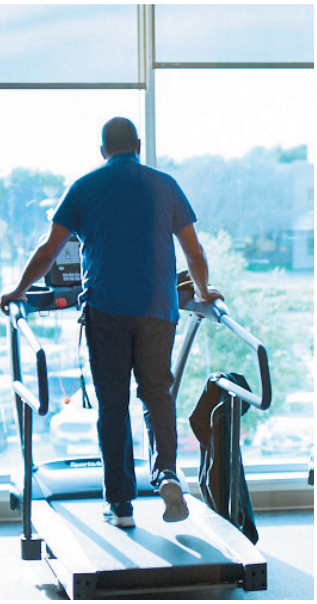

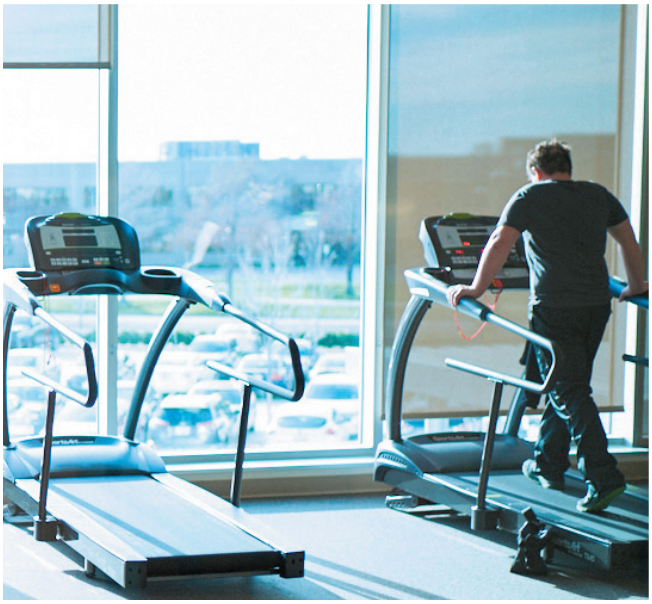

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