Study shows 'disastrous' damage in brains of retired CFL players

Hamilton Spectator teams up with scientists in landmark study on brains of retired football players.



Dr. Luciano Minuzzi couldn't believe the results of testing on retired CFL players. (JOHN RENNISON / THE HAMILTON SPECTATOR) By **STEVE BUIST** The Hamilton Spectator Wed., Aug. 30, 2017 Luciano Minuzzi had finished his very precise and very complicated analyses of brain scans from dozens of retired CFL football players and healthy volunteer subjects. Now it was time to look at the results.

As Minuzzi performed his calculations, he was blind to the subject's identity — a key part of the scientific process. He didn't know if he was examining the brain of a retired player or a control subject.

For each of the subjects, Minuzzi was analyzing the thickness of the brain's cortex — the thin outer shell of the cerebrum where the bodies of billions and billions of nerve cells reside. It's also the part of the brain that smacks the inside of the skull during a concussion.

Read more: <u>What happens in a concussion?</u>

When the results were unlocked and Minuzzi was able to compare the retired players to the controls, he was stunned.

Everywhere he looked, it seemed, the cortex of the players, on average, was significantly thinner than it was for the controls — whether it was the top of the brain, the front, the back, the sides and even the inner surfaces down the middle.

A thinning of the cortex is important because it suggests a substantial loss of nerve cells, supporting cells or both.

His first reaction?

"When I saw the images, I thought that must be wrong," said Minuzzi, a brain imaging expert and a clinical psychiatrist at McMaster University and St. Joseph's Healthcare. "I must have done something wrong.

"So I did it again."

And again. And again. And again.

Minuzzi went back and re-analyzed each subject four times because he couldn't believe what he was seeing. Each time, his results were confirmed.

On average, about 65 per cent of the cerebral cortex showed significant thinning in the CFL players. That's a staggering amount of damage that has accumulated in the players over time.

By comparison, Minuzzi said when he analyzes patients suffering some types of brain disorders, there might be five per cent of the cortex which shows significant thinning.

Minuzzi said the cortical thinning experienced by the players are "very, very strong results that we were not expecting."

"It's almost like seeing the brains of much older people," said Minuzzi. "They are not matching in terms of age.

"I was shocked," he added. "There's something really serious happening."

Minuzzi is part of the research team for <u>the Spectator</u>'s CFL concussion project, a unique collaboration between the newspaper and six researchers from McMaster University.

The project, which took more than two years to complete, involved comprehensive testing of 22 retired CFL players and another 20 healthy men of similar ages with no history of concussions who acted as control subjects.

Using a variety of sophisticated tests, the goal of the project was to examine the long-term effects of concussions and repeated hits to the head suffered by former football players.

The dramatic amounts of cortical thinning weren't the only horrifying results to emerge.

The retired players also underwent electroencephalogram (EEG) testing to measure the strength of the brain's electrical activity as they paid attention to different stimuli, again compared to healthy volunteers.

In some cases, the EEG results from players were no different than the results that would be seen in some types of coma patients.

The findings are almost hard to believe, said John Connolly, a McMaster professor and the Senator William McMaster Chair in Cognitive Neuroscience, who specializes in EEG analysis and concussions.

"In the coma patient, you can understand it — the person has had a catastrophic brain injury of some description," said Connolly, a member of the project's research team.

"But these men we tested are living their lives, they probably drove themselves here, some of them are running businesses.

"I'm not suggesting they're in a coma, quite the contrary," he added. "They came in, we chatted to all of them.

"Are there ways they're getting around this? I think there must be.

"There must be some way they're compensating for what amounts to a really disastrous attentional problem."

The disturbing differences found between the players and controls throughout the various forms of testing suggest strong evidence of a link between football, repeated hits to the head and long-term effects on the brain.

The findings raise very serious concerns about the future health prospects of former football players.

"It seems that their brains are already very fragile," said Minuzzi.

"The saddest part of this is that if the cortical thinning has been caused by neuronal loss, once those cells are dead, they are dead," he added.

"It's not something where we can do physiotherapy and recover, like a muscle can be increased with exercise."

Michael Noseworthy, an MRI imaging expert and part of the research team, said he too was shocked by the results.

"These players are unquestionably abnormal compared to the normal population of the same age," said Noseworthy, director of McMaster's School of Biomedical Engineering and director of Imaging Physics and Engineering at St. Joseph's Healthcare.

"I feel really bad for these players," he said. "And the current players, too."

Noseworthy was asked if there's any chance the players' results aren't connected to football.

"No, this is football," he said. "That's the common denominator."

The findings from this project are believed to be the first ever to report such a wide array of brain imaging and EEG results from living former professional football players.

"I've never seen a study that's done what you've done," said Robyn Wishart, a Vancouver-based lawyer who specializes in the litigation of brain trauma cases involving athletes. "It's mind-blowing what your images show."

Wishart has launched two separate lawsuits against the CFL on behalf of more than 200 former players who allege the league's negligence caused them to suffer brain injuries.

The project's findings raise grave questions about the safety of a dangerous sport that is popular precisely because of its violent nature.

"The players are getting stronger and faster and that's just adding to this issue," said Bob Macoritti, a study participant who played six seasons, mostly with Saskatchewan, in the mid to late 1970s.

"You can't get stronger, faster and heavier and not have more damaging collisions."

The research results, Wishart said, will help parents better understand the risks of the sport for their children.

"I think the parents have a right to know what a long career in the sport of football could mean to the long-term health of their child," she said.

When the NFL agreed last year to a \$1-billion settlement of lawsuits related to brain trauma, the league acknowledged as many as 6,000 former players may develop Alzheimer's or other forms of dementia.

Research into concussions and their connection to sports is now an area of growing interest across North America.

A long-term study of concussions and CFL players has been underway for more than two years at Toronto's Krembil Neuroscience Centre, which is affiliated with Toronto Western Hospital and the University of Toronto.

In addition to brain imaging research of living retired players, the Toronto project is also analyzing the brains of deceased players that have been donated for the study of CTE.

By virtually every measurement examined in the Spectator project, the retired players' results were worse than those of the healthy control subjects.

In many cases, the results were shockingly worse.

Here's what we found:

MRI

Magnetic Resonance Imaging is a method of using very strong magnetic fields to generate highly-detailed images of organs and tissues. It's particularly well-suited to looking at the brain.

MRI can show in real time which areas of the brain are activated — and how much activation is taking place in those areas — during the resting state or when tasks are being performed during the scans.

One main use of MRI scans is to look at so-called "white matter tracts" in the brain.

These are the various bundles of nerve fibres — much like electrical cables — that join different areas of the brain and distribute the signals between nerve cells.

Some of these tracts join the two halves of the cerebrum through a broad C-shaped band in the centre called the corpus callosum, and some of the tracts join together different areas within each half of the cerebrum.

Damage to these bundles could interfere with brain function or processing speed.

Four different types of analyses were applied to the MRI data and each analysis looks at different measures of the structural integrity of the nerve fibres that connect various areas of the brain.

The MRI analyses showed significant differences between the retired players on average and the controls in a number of white matter tracts across the cerebrum.

The testing showed 95 per cent of the players had decreased activity in a part of the prefrontal cortex believed to be associated with decisionmaking, when compared to an average level of activity in the control subjects.

The area showing the most consistent differences across all measures was the corpus callosum, the large band that connects the left and right halves of the brain. The differences seen in the retired players suggest two separate issues at work.

The first is that the nerve fibres in these bundles are showing signs of injury, degeneration, or the loss of the insulation around the fibres that help transmit the electrical signal smoothly.

The second is that large swaths of the corpus callosum showed signs of premature aging in the retired players compared to the control group.

Previous studies have shown the corpus callosum to be a common point of trauma in repetitive brain injuries. Because this large band connects the two halves of the brain, it can be damaged as the force of a blow is transferred back and forth through it, like a shock wave.

What's most disturbing about the results is that the differences seen in the retired players' brains were more consistent with the results that would be seen in someone who had just recently suffered a concussion.

Yet in the case of the retired players, it had been years — perhaps decades — since they'd last suffered a concussion or repeated blows to the head.

"For these players, with who knows how many concussive hits or subconcussive hits, it's pretty striking and clear that the damage has never been repaired," said Noseworthy.

The MRI scans also showed significant areas of premature aging in several of the white matter tracts that join areas within one hemisphere or the other.

The results also suggest that it's not necessarily the violent but less frequent concussive types of hits that cause the most damage.

Offensive and defensive linemen, who endure frequent but less violent blows to the head, showed greater damage to the white matter tracts of the brain than players such as receivers and defensive backs, who suffer higher energy hits but fewer of them. The results also showed that there was a significant and accelerated decline in the integrity of the white matter tracts as the age of the retired players increased.

CORTICAL THICKNESS

MRI scans can provide details about the brain's anatomy. This is useful for measuring the thickness of the cerebral cortex, the outer folded shell of so-called "grey matter" that covers the two halves of the cerebrum.

The cortex is made up of the bodies of billions of nerve cells, called neurons, which are responsible for organizing many of the higher-level functions of the human brain, such as memory, attention, emotion and problem solving.

Using some high-powered math, the thickness of the cortex can be calculated across the brain. A thinning of the cortex suggests either a loss of the neurons themselves, a loss of connections between the neurons, a loss of blood vessels that supply the nerve cells, or a combination of all three.

Cortical thickness is a very important measure because once nerve cells are lost, they can't be regenerated.

These were the most shocking of all our findings.

On average, the players had "significant" thinning in 65 per cent of their cerebral cortex area, compared to people in the control group.

Minuzzi, the psychiatrist and brain imaging expert, said he expected to see small spots of cortical thinning, perhaps localized to the areas where concussions occurred.

Instead, "they show global reduction," Minuzzi said. "The whole brain has been affected."

Some of the players are in their 40s, Minuzzi said, but "they have the brain of an 80-year-old, maybe 90-year-old."

The images from the players and the thinning of the cortex, he added, were "compatible to someone very old or someone with a neurodegenerative disorder.

"Something really wrong is happening here," he said.

"It's impossible to fake this. This is an objective measure of the thickness of your brain."

Altogether, the results showed, on average, that about 20 per cent of the mass of the cerebral cortex has been lost in the retired CFL players compared to the controls, which is a stunning amount of damage.

As Minuzzi studied the brain scans of the players, one image popped into his head — "the gladiators of the past," he said.

"People were cheering for someone to die," he said. "I was wondering if that's what's happening now when we turn the TV on.

"Are we seeing people who are being exposed to something that is quite negative that will change their lives forever?"

EEG

An EEG is a measurement of the electrical activity taking place across the brain.

While MRI imaging and cortical thickness analysis reflect the structure of the brain, EEG measurements help provide answers to the question of what functional consequences arise from these structural changes.

A series of 64 electrodes scattered across the outside of the skull pick up changes in electrical activity caused when nerve cells fire. The more cells that fire, the stronger the electrical signal.

In addition, an EEG is very good at picking up the timing of nerve cell activity in response to stimuli.

Our EEG experiment was designed to measure two different states how does the brain respond when a subject is consciously paying attention to stimuli, and how does the brain respond when a subject is not paying attention to the same stimuli?

In the first case, the subjects were told to pay attention to the sound of tones being played through earphones.

Most of the time, the tone was exactly the same and it was repeated over and over — beep, beep, beep, beep. The brain's electrical response to the regular tone dulls quickly as it becomes habituated to it.

But every so often, the tone would differ — perhaps it was longer, or louder, or a different pitch.

When the abnormal tone is played, the electrical activity spikes in response to this new stimulus.

It's well established from research that the electrical spike occurs around 300 milliseconds after the stimulus and this is called the "P300 wave."

Recordings from the electrodes allowed us to measure the size of the wave — which corresponds to the amount of electrical activity — and whether or not there was a delay in the response between the players and the controls.

In the second part of the experiment, the subjects watched a nature movie while the same beep-beep-beep tones were being played through their earphones. Again, the tone would differ every so often, as it did in the first part.

The subjects were told to disregard the background sounds of the tones and simply watch the movie.

But even though the subjects aren't consciously paying attention to the tones, the brain is still monitoring the sounds.

And the same process is at play — the response to the normal tones becomes habituated and there's a spike in electrical activity when the tone changes.

In this case, the phenomenon is known as the Mismatch Negativity effect, or MMN, and the spike occurs about 150 to 250 milliseconds after the abnormal stimulus.

Our experiment measured the conscious (P300) and unconscious (MMN) responses to the abnormal tones for the retired players and controls.

When consciously listening to the tones, the P300 responses of the players on average were only half as strong as the control group responses, regardless of whether the tone changed in pitch, length or loudness.

These results were highly statistically significant.

Since an EEG measures the strength of electrical activity, the results suggest there was considerably less firing of nerve cells, on average in the players' brains compared to the controls.

"You can have various theories as to what's going on, but it means that they cannot pay sustained attention," said Connolly.

For some of the retired players, there were no signs of P300 electrical activity shown, regardless of how the tone changed — a result that would be consistent with some types of coma patients.

"To show a P300 is not something only shown by geniuses or only people in peak physical condition," Connolly said. "Everybody shows this thing.

"But some of these fellows do not show P300s and that to me is simply stunning.

"It might be that someone has a reduced one or a delayed one but to not see it at all, I'd never seen that before, literally," Connolly added. "And I've been doing this for 30-plus years."

The players, on average, also exhibited a delay in response when the abnormal tones were louder or longer.

A delay in response suggests that it might be taking longer for the signal to be processed in the brain.

When subconsciously listening to the tones, the players' MMN responses were significantly reduced compared to the control group, particularly when the abnormal tones were longer or of a different pitch.

These responses come from areas in the brain that include the auditory (hearing) cortex and areas that control our ability to pay attention and focus.

Both the P300 and MMN responses are linked to different types of memory formation.

One possible explanation for the reduced strength of the electrical activity in the players is that the overall number of nerve cells in their brains has been reduced because of the cortical thinning that's taken place.

HEALTH AND DEPRESSION

All of the retired players and control subjects were asked to fill out a self-reported health survey, a concussion symptom survey, as well as the Beck Depression Inventory, a standardized test that can show if a subject exhibits signs of depression and if so, how severe it might be.

The health and symptom surveys asked subjects to rate themselves on more than a dozen measures, including general health, pain, emotional well-being, memory difficulties, sleep difficulties and irritability. The players' average score on the Beck Depression Inventory was nearly four times higher than the average for the control subjects.

Seven out of 22 players showed some signs of depression.

Not one of the 20 controls showed signs of depression.

When it came to the symptom scoring for measures such as irritability, difficulty in remembering and emotional sensitivity, the results were even worse.

The players' total concussion symptom scores were five times higher than the control subjects.

For every one of the six categories, the players scored worse than the controls.

What's most disturbing is that for many of the retired players, it had been years — if not decades — since they last suffered a concussion. In fact, a few of the players reported they had never been officially diagnosed with a concussion during their playing careers.

Yet on average, the players consistently reported the types of symptoms expected to be found in people who were recovering from a recent concussion.

The results were particularly dramatic when it came to self-reported problems with memory. The average symptom score was 10 times higher for the players than it was for the controls.

Sixteen of 22 players reported some level of difficulties with memory. Only two of 20 controls reported similar issues.

In all eight of the general health categories, the players' results on average were worse than those of the controls. The players were significantly worse in the pain and social functioning categories.

IMPACT TESTING

ImPACT, which stands for "Immediate Post-Concussion Assessment and Cognitive Testing," is a computer-based series of modules that measure motor processing speed, reaction time, visual memory, impulse control, and verbal memory.

This was the one aspect of our testing where the results were somewhat inconclusive.

The players performed worse than the controls in four of the six categories, but the differences were not statistically significant.

The players performed better than the controls in the visual memory and motor processing speed categories, which might be a residual effect of excelling in a sport that requires quick decision-making and the ability to remember visual patterns on the field.

Retired players who took part in the project have reacted with a mix of shock and unease at the disturbing results.

Most, however, also acknowledged they weren't surprised.

"It's a big eye opener," said longtime Ticat receiver Mike Morreale, now 46 and the youngest of the 22 players tested.

"What upsets me is that, generally speaking, my peers are suffering like that and it makes me feel very uneasy inside," Morreale said.

Former Argo Dan Ferrone, who played 12 seasons as an offensive lineman, said the results are "conclusive proof that football does have an impact on your brain matter."

"I think a lot of guys probably know they have damage," added Ferrone, now 59. "They're just not aware of how bad that damage is."

In addition to his 12 years playing professional football, he also played another nine years of high school and university football.

"That's a lot of abuse," he said.

Ferrone said he was diagnosed with one or two concussions during his career, but now suspects in hindsight he may have suffered as many as 10 concussions.

That's not unusual, given the findings of a joint Harvard-Boston University study published in 2015.

In a survey of 730 U.S. collegiate football players over one season, the study showed that for every one diagnosed concussion, there were 26 potential concussions that went unreported or undiagnosed.

"These results are clearly an indication of the trauma that can happen from this game, no question about that," said Don Bowman, a defensive back who played for Winnipeg and Hamilton in the mid to late 1970s.

"Where we go with this, I don't know.

"There are guys making an awful lot of money playing this sport and perhaps that's worth it," Bowman added. "It wasn't so much that way back when we were playing."

Bob MacDonald, an offensive lineman with Calgary and Hamilton in the early 1990s, admits he now wonders, "What have I done?"

"My job was to smash guys as hard as I can," said MacDonald, now a teacher at Saltfleet Secondary School. "So I never really gave it that much thought for a long time.

"When I was growing up, I never thought about impact and inertia and the brain flipping and flopping," he said. "You just think 'I'm wearing equipment, I'm safe."