









Key Points

- 1. Study looked at whether reduced intracranial compliance (in rats) made the brain more susceptible to injury/insults
- 2. Intracranial compliance is a measure of how the brain responds to an increase in volume
- 3. Research has shown that Chiari patients have lower compliance than normal and that surgery increases compliance
- 4. Study used a rat model to lower the compliance in rats prior to simulating repeated brain insults
- 5. Found that the rats with the lowest intracranial compliance had the largest metabolic changes in the brain
- 6. Many Chiari patients report their symptoms were triggered by a traumatic event
- 7. The role of trauma in triggering/aggravating Chiari symptoms is not well understood, but compliance may play a role

Definitions

compliance - a measure of a vessel's stiffness, mathematically expressed as dV/dP or change in volume per unit pressure

cranium - skull

dura - thick outer covering of the brain and spinal cord

intracranial - inside the skull

intracranial compliance (IC) compliance inside the skull

intracranial pressure (ICP) - the pressure of the fluid inside the

metabolism - all the processes by which the body breaks down food and releases and regulates energy

metabolite - a substance created during metabolism

Chiari Patients May Be At Greater Risk With Head Trauma

September 20, 2006 -- Because there is so little research published which directly applies to Chiari - at least compared to other diseases - sometimes we have to turn to related topics and try to leverage the research in that space and apply it to our disease. For example, Chiari & Syringomyelia News has published articles on topics ranging from acupuncture to the impact of chronic pain on the brain, which while they involved zero Chiari patients, were nonetheless very relevant to our community.

A similar such study was published recently in the August, 2006 issue of the journal, Neurosurgery. In it, an international team led by Konstantin Salci of Uppsals University, Sweden, show that low intracranial compliance may leave the brain vulnerable to traumatic injury. While the thrust of the work relates mainly to the management of traumatic brain injuries, regular readers of this newsletter will recognize some scientists believe compliance plays an important role in Chiari as well.

Compliance is a measure of a vessel's, or container's, stiffness, and essentially is a measure of how well a container can handle an increase in volume. A highly compliant container, like a balloon, can be expanded by blowing air into it. A low compliance container, like a glass jar, will not expand much as the pressure inside it is increased.

Thus intracranial compliance refers to the compliance of the contents of the skull, which essentially acts as a vessel for the brain, blood, and cerebrospinal fluid. When the heart beats, blood rushes into the brain. To accommodate this extra volume, blood and CSF are forced out of the brain compartment into the spinal area. During the second phase of the cardiac cycle, this process is reversed and CSF flows back into the brain from the spinal area.

Intracranial compliance represents, in one sesne, how well the brain handles this cyclic inflow of blood driven by the heart. With Chiari, the herniated tonsils block the natural outlet for CSF and studies have shown that Chiari patients tend to have lower intracranial compliance than normal. In addition, it has been shown that successful decompression surgery results in an increase in intracranial compliance. Thus, with Chiari linked to low compliance, any research on the ramifications of low compliance becomes interesting to the Chiari community.

In this study, Salci and his colleagues used a rat model to demonstrate that rats with lower intracranial compliance suffered greater effects from subsequent brain insults (physical insults, not the verbal kind). Specifically, the researchers took a number of rats, removed parts of the skull and exposed their dura (see Figure 1). Next, in some of the rats, they dropped a weight on to the exposed dura to cause swelling. They then replaced the skull pieces but on some of them glued layers of rubber on the inside of the bone. The rats randomly received 0,1,2, or 3 layers of rubber, which incrementally reduced the space available for the brain to expand. The goal of all this work was to reduce the intracranial compliance of some of the rats by varying degrees.

After the compliance lowering work, some of the rats were chosen to get repeated injections of saline which were infused into their brain compartments. This infusion of fluid into the brain was intended to test the effect of the reduced compliance (which recall is the ability to handle an increase in volume). Finally all the rats were euthanized and their brains examined to measure the levels of specific substances known as metabolites. Metabolites are by-products of the body's natural metabolism and abnormal levels in the brain can indicate disease or damage.

The researchers found that the rats with the lowest compliance (three layers of rubber) had the most significant metabolic changes in their brains. While this was purely a chemical change, in other words the real-world effects of these changes were not evaluated, it is interesting that when the brain loses its natural compliance it loses its cushion, so to speak, to absorb certain events.

It is certainly a long way from a rat model of trauma to Chiari patients, but it is worth noting that many people report that trauma triggered their Chiari symptoms. In fact, Milhorat's well known study found that 24% of Chiari patients identified some type of trauma as a precipitating event.

Anecdotally, one of the most common questions Conquer Chiari receives is whether car accidents, falls, and blows to the head can "cause" Chiari. While Chiari is most often congenital, what sparks, or aggravates, symptoms is not fully understood, and the mechanism that might link trauma to Chiari symptoms remains a mystery. Could it be that people with Chiari have lower compliance which makes the effects minor traumas more pronounced?

The Chiari exertional headache is well known, but what some might not realize is that there are some indications

saline - salt water adjusted to match the normal levels in the human body

cerebellar tonsils - portion of the cerebellum located at the bottom, so named because of their shape

cerebellum - part of the brain located at the bottom of the skull, near the opening to the spinal area; important for muscle control, movement, and balance

cerebrospinal fluid (CSF) - clear liquid in the brain and spinal cord, acts as a shock absorber

Chiari malformation I - condition where the cerebellar tonsils are displaced out of the skull area into the spinal area, causing compression of brain tissue and disruption of CSF flow

decompression surgery -

general term used for any of several surgical techniques employed to create more space around a Chiari malformation and to relieve compression

Source

Salci K, Nilsson P, Goiny M, Contant C, Piper I, Enblad P. <u>Low</u> intracranial compliance increases the impact of intracranial volume insults to the traumatized brain: a microdialysis study in a traumatic <u>brain injury rodent model.</u> Neurosurgery. 2006 Aug;59(2):367-73 that heavy labor type jobs, or extreme activities such as skydiving, may play a role in Chiari symptoms. Perhaps the low compliance that research indicates exists with Chiari means the brain also can not handle the physical side effects of sustained and repeated physical activity.

While the answers to these questions lie in the future, the National Institutes of Health recently awarded a significant research grant to study the clinical implications of compliance in Chiari, so the future may arrive sooner than we think.

Figure 1 Experimental Design

- 1. The dura is exposed surgically on all rats
- 2. Some rats are subjected to a weight drop on the exposed dura
- 3. Skull pieces are replaced with 0-3 layers of rubber glued to the inside to reduce the volume space of the cranium, thus lowering the compliance
- 4. Some rats were given repeated saline injections to increase fluid/volume in the brain
- 5. Rats were euthanized and examined for levels of specific brain metabolites

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