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**Long Term Effects of Concussions and the Frequency of Injury to the
Different Regions of the Human Brain**

By

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An undergraduate honors thesis submitted in partial fulfillment of the requirements for

the degree of

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Thesis Advisor

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ABSTRACT:

Concussions, or mild traumatic brain injuries, do not have a universally accepted definition but there are key features that the experts agree upon; most notably that they are caused by a direct blow, they cause functional disturbances, and that they cannot be explained by another injury or impairment. Most concussions are resolved within a few days but 10-20% have lingering effects that can last for years. In this study, frequency of lingering injury to each brain region was determined from data from thirteen studies and compared to Scheid et. al's frequency of short term injury by brain region using ANOVA testing. No significance was found in the difference in frequency of injury by region between long term and short term concussions (p -value=0.717, n =10, α =0.05). This suggests that regions either heal at the same rate or can all be compensated for. Further research is needed to determine the pathophysiological root of the long-term effects of concussions.

INTRODUCTION:

As of 2018, there is no universally accepted definition for a concussion, however there are five key features of a concussion that have been agreed upon by experts. Firstly, a concussion is caused by a direct blow either to the head itself or to the body that sends an impulsive force to the head; this may or may not cause unconsciousness (Halstead 2018). The concussion results in normally short lived impairment to neurological function; however, in some cases, these impairments linger for longer (Halstead 2018).

The symptoms and signs must reflect a functional impairment and not a structural one; they also cannot be explained by any other injury or impairment, i.e. alcohol or medicine (Halstead 2018). Giza et. al did a synthesis of over 100 research papers to find that the pathophysiological pathway following mild traumatic brain injury (mTBI) includes “abrupt neuronal depolarization, release of excitatory neurotransmitters, ionic shifts, changes in glucose metabolism, altered cerebral blood flow, and impaired axonal function” (Giza 2014). These factors can cause a series of imbalances and by default cause numerous symptoms. Such symptoms can be broken down into the following categories: sleep, vestibular and/or oculomotor, cognitive, somatic, and emotional (Halstead 2018).

Patients are often followed up with up to a month depending on the severity of their concussion, however that is where most research ends. We do know about second hit syndrome and post concussion syndrome but further research is necessary to understand the long term effects of concussions on cognitive function. This is especially vital for contact sport athletes who often receive multiple concussions over the course of their career. A committee on sports related concussions in youth determined that approximately 10-20% of those with concussions experience symptoms for weeks, months, or years after the initial hit, they refer to this as Post-concussive syndrome (Rivara 2014). However, given the nature of concussions and the brain, currently the only treatment option is symptom management.

In most cases, the patient does not undergo any imaging to determine which region of the brain was injured, as long as symptoms can be managed. D'souza MM et. al used diffusion tensor tractography to look at the brains of patients with traumatic brain injury to try to determine the regions of the brain that were injured. They found that their new technique also matched with the results of the Rivermead Postconcussion Symptoms Questionnaire (D'souza 2015). This opens up the possibility of determining where the injury is located and with further research, customizing treatments to the region or in cases of severe damage, developing therapies to help reestablish neuron connections in the region.

Most long term testing is based on rating scales that compare the patient to established healthy controls. These tests have found that many common long term symptoms of concussions include decreased psychomotor function, decreased executive function, decreased global cognitive ability, decreased intelligence, poor memory, difficulty comprehending language, decreased perception, and inability to concentrate or pay attention (Cunningham 2020). The majority of studies use a variety of tests that differ from study to study, leading to different symptoms being identified as a long term effect of concussions.

As previously mentioned, while the field of neuroscience, especially around concussions is expanding, there has not been enough emphasis on the long-term effects of concussions. We can see in the real world-- watching athletes retire younger or never playing quite the same following a traumatic head injury-- that concussions have a

lingering effect and repeated concussions amplify the effect. While some research has been done, we still do not have a proper treatment plan to help prevent traumatic brain injuries or slow/stop the long term effects.

This leads to the question, what are the long term effects of concussions and how do they affect quality of life? Are certain regions of the brain more likely to be subject to long term injury following a traumatic brain injury? Given that there is a bias in who the studies have historically been on, I hypothesize there will be a higher frequency of injury to the frontal lobe as it is most likely to be impacted in the case of a fall or hit.

METHODS:

Subjects and Criteria for Inclusion:

All data has been compiled from thirteen articles from the period of 2009 to 2020. Articles were obtained from PubMed, Ebsco, Web of Science, Science Direct, and BioOne databases. Articles had to follow up with subjects a minimum of two months following concussion and not rely entirely on self surveys to ensure uniformity and reliability between articles used in analysis (Figure 1). Diversity in research topics was permitted to prevent bias towards any one region of the brain.

Athletes and military personnel are the highest represented groups due to the frequency of concussions in these groups, athletes being the sole subjects of five of the articles. Little information was available in papers used on the demographics of the patients utilized in their studies due to confidentiality rules.

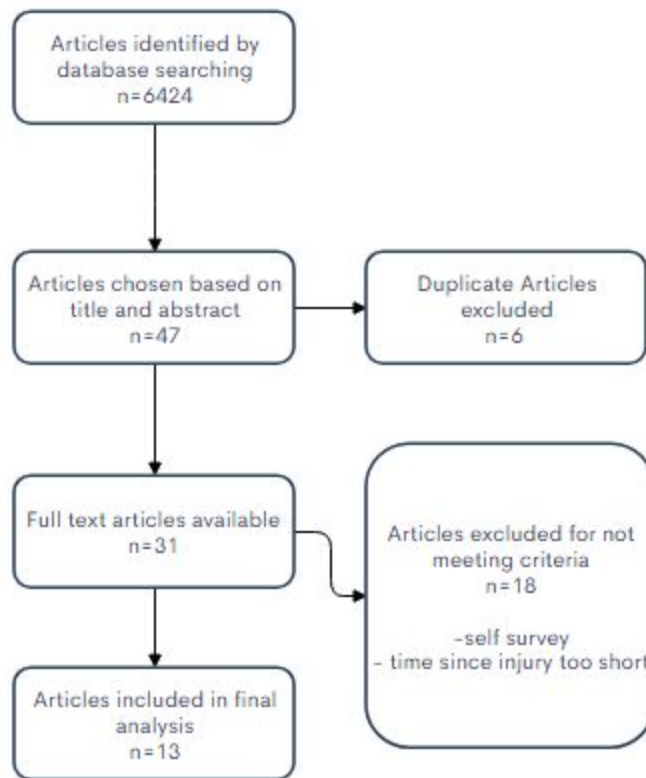


Figure 1: Flowchart of search method

Procedure:

Each paper was read in entirety for length of time before resurveying patients, number of patients surveyed in study, and symptoms reported by authors. Symptoms were compared to an established list of brain regions' functions and related symptoms (Table 1) to determine the region of the brain most likely injured. Regions of the brain used for comparison were the cerebellum, the brain stem, the frontal lobe, the parietal lobe, the occipital lobe, the temporal lobe, the hypothalamus, the pituitary gland, the

thalamus, and the basal ganglia. Multiple regions may have some control over the same processes; if specifics on symptoms allowed for determination of the most likely injured region, the suspected region was listed as injured region. If unable to determine specifics of symptoms, all possible regions were listed and counted equally.

Table 1: Regions of brain, their function, and related symptoms used for comparison to long term studies in this study.

Region	Use	Examples of Related symptoms
Cerebellum	Proprioception, Movement	vertigo, ataxia, nystagmus, intentional tremor, slurred speech, hypotonia, exaggerated broad based gait, dysdiadochokinesia
Brain stem	autonomic function (sleep wake cycles, breathing, heart rate, temperature, digestion, sneezing, coughing, vomiting, swallowing)	insomnia, abnormal sleep patterns, balance issues
Frontal lobe	personality, behavior, emotion, judgment, planning, body movement, speech, intelligence, concentration, self awareness	sudden change in behavior, impaired judgment, memory loss, reduced motor skill and spatial reasoning, inability to interpret social cues
parietal lobe	language, sense of touch, pain, interprets temperature, interprets vision, hearing, motor, sensory, and memory, spatial and visual perception	inability to form speech with clear understanding, inability to interpret senses
occipital lobe	interprets vision (color, light, movement)	color blindness, decreased dimensional awareness, decreased spatial awareness
temporal lobe	understanding language, memory, hearing, sequencing and organization	unable to understand language, memory loss
hypothalamus	autonomic control (hunger, thirst,	erectile dysfunction, high/low blood

	sleep, sexual response, temperature regulation, blood pressure, emotions, hormone secretion)	pressure, sudden change in behavior, hormone imbalances
Pituitary gland	endocrine glands (hormones that control sexual development, bone growth, muscle growth, stress)	hormone imbalances, stunted growth
thalamus	pain sensation, attention, alertness, memory	memory loss, attention disorders, inability to concentrate
basal ganglia	fine motions	loss of fine motor control

Statistical Analysis:

Using data obtained from articles, the frequency of injury to each brain region long term was obtained. An ANOVA test was utilized to compare these frequencies to the frequency of injury to each brain region immediately following injury. An alpha value of 0.05 was used.

RESULTS:

The order of frequency of sustained injury by brain region was found to be--in order-- frontal lobe (45.21%), parietal lobe (17.81%), cerebellum (10.96%), thalamus (9.59%), brainstem (8.22%), temporal lobe (4.11%), basal ganglia (1.37%), pituitary gland (1.37%), hypothalamus (1.37%), and occipital lobe (0%).

When comparing the long term frequencies (Table 2) to established short term percentages using an ANOVA test, a p-value of 0.717 ($n=10$, $\alpha=0.05$).

Table 2: Frequency of injury to each brain region

Region	Count	% total of listed symptoms-long term	% total-short term
Cerebellum	8	10.95890411	1.68
Brain stem	6	8.219178082	1.008
Frontal lobe	33	45.20547945	50.42
parietal lobe	13	17.80821918	11.76
occipital lobe	0	0	3.36
temporal lobe	3	4.109589041	18.48
hypothalamus	1	1.369863014	0
Pituitary gland	1	1.369863014	0
thalamus	7	9.589041096	0.504
basal ganglia	1	1.369863014	5.88

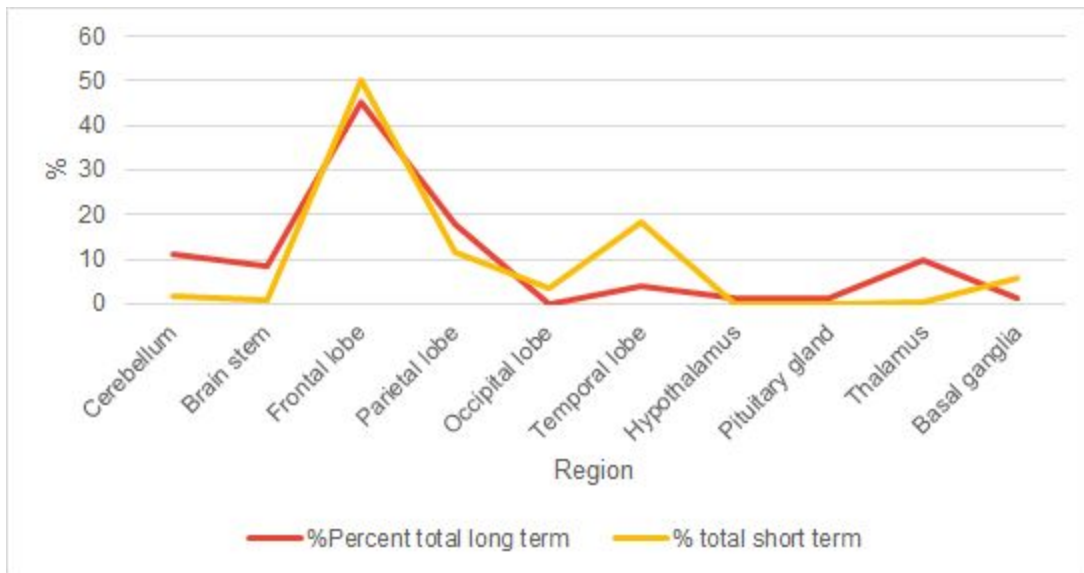


Figure 2: Graph of differences between frequency of injury by region long term vs short term

DISCUSSION:

The results show that the frontal lobe has the highest frequency of long term injury, supporting the hypothesis. However, the ANOVA test shows that the frequency of long term injury to all regions falls in line with the frequency of initial injury (Figure 2). This means that the recovery rate by region is expected to be the same.

This study was limited by the fact this is a meta-analysis. Some anecdotally known long term concussion symptoms, for example tinnitus, were not included in any of the articles used. As noted earlier, many regions of the brain contribute to the same function. While this is incredibly useful in cases of injury-- as other regions can sometimes compensate for the damaged region--, it does complicate full understanding of the injury without full medical imaging of the brain and testing of function. However, given the insignificance of the p-value comparing long-term to short term, the presence of this data may not have had much effect on the result (Scheid 2003).

Work is being done short term to better technologies used for diagnosing traumatic brain injuries, such as D'souza et. al's work on diffusion tensor tractography (D'souza 2015). As new technologies are created, there is hope that concussions can be properly diagnosed and treated to help prevent long term effects. Future studies could utilize these diagnostic tools to replicate this study and identify what causes the long term effects post concussion. A better understanding of location of concussions could help find correlations between other mental disorders as well; for example, McKee et. al have found evidence in members of the military that post concussion syndrome, post traumatic

stress disorder, and chronic traumatic encephalopathy may share a biological root based on their clinical and pathological features (McKee 2014).

Further studies on concussions and how they change the pathways in the brain are necessary to find treatment options. Using MRI or other imaging tests can help determine where the injury is and why it is causing the symptoms afflicting the patient. Overall, what is most important is helping the patients and ensuring the best quality of life for them. Better understanding of which regions are injured can improve the number and quality of treatment options.

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