4-30-2021

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Recommended Citation

Ballinger, Dominique, "Meta-Analysis of Long Term Executive Functioning Deficits in Individuals with Mild Traumatic Brain Injuries" (2021). *Neuroscience Honors Papers*. 14.
https://digitalcommons.ursinus.edu/neuro_hon/14

Meta-Analysis of Long-Term Executive Functioning Deficits in Individuals with Mild Traumatic Brain Injuries

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Abstract

The epidemic of traumatic brain injuries (TBI) has grown throughout the years and has continuously increased. As of 2020, the incidence rate for TBIs was approximately 12% of the population (Frost 2020). Within these traumatic brain injuries, researchers have found a system of categorizing TBIs based on severity of symptoms between mild, moderate, and severe. Mild TBI (mTBI or concussion) is a highly prevalent injury. In 2013 alone, 31.5 for every 100,000 individuals were found to have suffered from a mTBI, with an exceedingly immense proportion between the ages 12 to 18 years old (Selassie, 2013). Just four years later the CDC found an increase in prevalence to about 15% (around 2.5 million) of youth (DePadilla 2017). Within this meta-analysis, the goal is to establish consistency and understanding on the longevity of executive functioning deficits that arise after an mTBI. There are inconsistencies when establishing significance of cognitive deficits among individual studies, however, this study was able to establish a significant model estimate when comparing concussed to non-concussed individuals on an array of methods. Predominately all subcategories with each covariate presented high percentage in strong/moderate effect size range, as well as significance between concussed and non-concussed individuals. These significant differences present a more comprehensive pattern in order to distinguish the executive function deficits. When looking at various studies there are irregular results, but comprehensive meta-analysis provides a clearer picture for the cognitive deficits, which is thereby a strength for the meta-analytical approach. With that being said, there is substantial evidence to the severity of this injury, and this meta-analysis thereby provides evidence towards implementing better education, understanding and research on this epidemic of mTBI.

Introduction

Prevalence and Categorization of Traumatic Brain Injuries

The prevalence of traumatic brain injuries has continuously grown over the years. As of 2018, there was an estimate of 69 million individuals who have suffered from a traumatic brain injury (TBI). However, globally, TBIs were found to have an incidence rate of approximately 12% (Frost 2020).When diagnosing and gathering the statistics regarding these injuries, the CDC distinguishes the rates within our country based on TBI in relation to hospitalizations, emergency department (ED) visits, and/or deaths. As of 2014, the CDC found 2.87 million TBIs related to hospitalizations, ED visits and deaths in total. While that is an astonishing number, the fact that 837,000 of those individuals were children is more eye opening (CDC). Within the CDC databases, the statistics are displayed amongst an array of different variables. The database initially focuses on the injury in relation to hospitalization, ED visits, or death. These categories are chosen to be abbreviated as EDHD. In conjunction with the categories above, the causes of injury are also surveyed, which included anywhere from falling to a motor vehicle accident. Each of these variables are based on ten age groups broken down by approximately 10-year intervals. The most at risk for TBIs were found to be 0-4, 15-24, and greater than 75 years of age. Through further analysis, the cause of injury is seen to vary widely between age groups. Older adults and young children’s injuries were attributed to falls, while the adolescents to middle ages adult injuries were a result of predominantly motor vehicle accidents and unintentionally being struck by/against an object (CDC). Due to the high prevalence of injury during childhood and adolescence there are organizations that strive to promote awareness on severity of brain injuries during the early years of life. HEADS UP is a CDC run educational organization that provides learning materials, training, and parental resources about the criticalness of minimizing risk of brain injuries (CDC). This organization, among several others, aims to raise awareness for these injuries, however there is still inconclusiveness regarding classification and understanding of this broad injury.

Categorization of Traumatic Brain Injuries

Traumatic brain injuries are found to vary widely in severity, and thereby make diagnosis indeterminate at times. Classification of TBIs can be encapsulated into three categories: mild, moderate and severe, based largely on symptomatology. The distinguishing factors between severity can be ambiguous to decipher. The categories are found on a continuum rather than partitioned into set types. The mild to moderate TBIs can generally be deduced by a brief lapse in mental functioning. Contrastingly, severe TBI is described as a longer lapse in mental functioning, along with the potential for memory loss (NIH). The CDC recently identified four groups of symptoms that can be examined when patients suffer from a TBI. Physicians will look at thinking/remembering (cognition), physical, emotional/mood and sleep. Within these 4 groups, there are subcategories to further analyze cognitive functioning more clearly. The subcategories consist of a subset of criteria, which include:

Table 1: *Subcategories of symptomatology for traumatic brain injuries*. Adapted from Center for Disease Control and Prevention (CDC)

Thinking and Remembering	**Physical**	**Emotion/mood**	**Sleep**
Difficulty concentrating	Headache/Dizziness/ Fuzzy/Blurry vision	Anxiety/ nervousness	Sleeping less
Difficulty thinking	Feeling tired and no energy	Irritability	Sleeping more

Feeling slowed down	Nausea or Vomiting	Sadness	Trouble falling asleep
Difficulty retaining new information	Vestibular Issues (Balance, sensitivity to noise of light)	More emotional	

In order to better distinguish symptoms for all levels of severity for TBIs, researchers have been able to institute these criteria. Nevertheless, these symptoms are constantly evolving and adapting as more information is revealed regarding traumatic injuries to the brain. Mild TBIs (mTBI), commonly synonymous with a concussion, is a highly prevalent injury. One of the most common mechanisms for mTBI is from sports-related injuries. In 2013 alone, 31.5 for every 100,000 individuals were found to have suffered from a mTBI, with an exceedingly immense proportion between the ages 12 to 18 years old (Selassie, 2013). Just four years later, the CDC was able to find an increase in the rate of injury to about 15% (around 2.5 million) of youths suffering from at least one mTBI and about 6% having endured two or more concussions (DePadilla 2017). Brain injury during these crucial age ranges could easily stun or alter neurological or behavioral development. Researchers have used various techniques to determine the longevity and best recovery plan for these injuries, nevertheless, the correct answer has yet to be determined.

When suffering a mTBI there are a considerable number of symptoms that are quickly displayed within individuals. These symptoms can be encapsulated within the 4 categories determined by the CDC and other health organizations (Table 1). General symptomatology that has been reported shortly after are headache, confusion, lightheadedness, blurred vision, sleepiness, trouble with memory or attention, and sensitivity to light, among others (Eunice 2016). The duration of symptomatology after suffering from a mild-TBI are variable. A prospective cohort study of approximately 300 patients from the age of 11 to 22 were examined to determine the incidence, duration and potential treatment regimen after a mTBI. The study found that headache, dizziness, fatigue, and cognitive issues were initially experienced shortly after the incidence. However, forgetfulness, frustration and sleep disturbance were observed during a follow up after the injury. When further analyzing the duration of the following symptoms, researchers established a median duration of about 2 weeks, while blurred vision, dizziness and nausea were more transient symptoms. Most importantly, this cohort study found about 25% of participants experienced cognitive impairments, headaches and fatigue after more than a month following the incident (Eisenberg 2014). It is critical to note that cognitive impairments, headaches and fatigue have been found with a longer duration in regard to symptomatology, thereby making them critical for physicians to focus on when providing treatment regimens. The CDC suggests that the best form of recovery is cognitive rest. With this type of rest, it is said that not only is your body physically resting but you are refraining from utilizing technology and other cognitively stimulating things. Researchers have found that increasing the amount of cognitive activity while recovering from a mTBI can result in elongated periods of recovery (Brown 2014). Cognitive rest can be a rather ambiguous term; therefore, proper treatment regimens need to be researched.

Long-term consequences of mTBI

There has been research exhibiting a strong association between mTBI and long-term deficits in executive functioning when compared to peers who have not sustained any injury to the brain. Scientists have found that completion of the Attentional Network Test and the Task-Switching Test yield consistent results from 72 hours to 2 months after suffering from a concussion (Howell 2013). These tests were able to determine not only the significance between the concussed and control groups but the longevity for this injury. Further research has been done to expand the modes of understanding these deficits more succinctly.

There are several approaches to measure cognitive functioning and more specifically, executive functioning deficits, these include self-report/ surveys/ questionnaires, cognitive or behavioral neuropsychological exams, and neuroimaging. Researchers used both neuropsychological evaluations and behavior rating inventory of executive functioning (BRIEF) questionnaire to investigate the inadequacies in children after suffering a concussion. Mangoet's lab found that children up to 5 years post-injury, had significant deficits in the BRIEF scale, specifically within the neuropsychological measures (Mangoet 2002). Each of these studies provide an approach to investigating these deficits. They additionally allow for better understanding of the best methods when studying mTBI. Depending on the goal of the study and the desired variables that are being investigated, the methods adopted in modern mTBI studies present various pros and cons.

When comparing the strengths and weaknesses of self-report and neuropsychological evaluations, subjectiveness and objectiveness respectively of these said measures, are commonly discussed. Investigating the effectiveness of self-report forms, there are several pros and cons that are examined. First and foremost, one major pros for self-report are that it can be administered in large samples. Additionally, it allows the patient, who is more in touch with the topic in question, to respond to things that may not be seen at surface level. The cons, on the other hand is primarily in regard to the fact that the report is very subjective. The participant could interpret the question in several different ways. Additionally, within these self-report forms there is opportunity for social desirability bias and response bias. Each of these biases leads the person to choose the answer that is "right" or "most accepted" (Demetriou 2015). Due to the subjectivity of these measures, neuropsychological tests provide an objective method of assessing the deficits seen post-injury. These objective measures can assess various factors neurologically and allow for the distinction between them. A major con to this method is that it is hard to eliminate confounding variables of the different neurological functions being evaluated (McCrory 2005). Advantages and disadvantages regarding these techniques are important to consider when trying to increase validity and generalizability within a study. There are several ways of using these methods that must be considered when formulating hypotheses and experimental measures in order to provide the most thorough analysis.

When connecting the assortment of methods to the symptomology, the analysis for the duration of symptoms often requires distinctive techniques. These tasks can differ greatly in reliability. When assessing the majority of the physical, emotional, sleep symptoms typically those pertain to more subjective Likert scale ratings from the individual. On the contrary, when assessing difficulty thinking/remembering (cognition) and other physical symptoms neuropsychological tests are commonly used due those being more objective symptoms to assess. However, these ideas have yet to be sufficiently understood and require further verification. While Howell and Mangoet's teams were able to find deficits among concussed individuals, there is still an immense amount of inconsistency within this topic of investigation. Howell found there to be differences between groups using neuropsychological testing, Mangoet was unable to distinguish any significance through the use of neuropsychological evaluations. These inconsistencies between studies makes it harder for the scientific community to fully ascertain a comprehensive understanding of this injury. With this irregularity it is paramount to continue the investigation of mTBIs.

Within this field of research, the self-report forms, questionnaires and neuropsychological evaluations plaque the investigatory process. Neuroimaging is a technique that can be used when studying brain injuries and cognitive deficits. Within the realm of studies that utilize neuroimaging techniques, there are both functional and structural imaging techniques. Structural strictly photographs the brain to allow visualization of various brain structures. These techniques consist of CT scans, MRI, and PET scans. Each of these methods of imaging are very good at visualizing predominant regions of the brain. However, structural techniques are not often used to assess mTBI. This is primarily because the impact of injury does not normally cause macroscopic damage that can be distinguishable on the structural scans. Due to the following limitations, functional neuroimaging techniques are used to evaluate the level of deficits if any. Common functional neuroimaging techniques consist of fMRI, fNRI, EEG, and diffusion-tensor imaging. Each of these techniques measure brain activity in specific regions of the brain while simultaneously measuring performance on different neuropsychological tests that analyze executive functioning. This duality of functional techniques provides a preferred method for analyzing deficits post incident.

Numerous researchers were able to find impacts within the dorsolateral prefrontal cortex (DLPFC) when using these techniques. The link between the DLPFC and executive control is an association of structure and function that has been studied for years. Researchers proved this link several years ago by lesioning the DLPFC region comparing performance on Wechsler Adult Intelligence Scale (WAIS) and subtests of the Delis Kaplan Executive Function System (D-KEFS) with control individuals. Results proved that those individuals with DLPFC lesions were significantly impaired in the WAIS and D-KEFS test. These tests both examine frontal lobe functioning and more importantly executive functioning (Barbey 2013). With this association deciphered, it raises the question of how we may be able to link observation of these cognitive deficits to activity within the DLPFC region. To attempt to answer this question, it begins with the emerging field of functional neuroimaging. A study of 8 college level football players showed evidence of increased blood oxygen level dependent (BOLD) readings when undergoing a fMRI post-mTBI in comparison to their baseline fMRI, as well as, to those who never had suffered a mTBIs. The increased BOLD levels indicate required extension into neighboring neuronal networks to perform the same cognitive tasks as controls. The increased BOLD levels when performing cognitive tests shows an imperative association that is crucial to explore further (Jantzen 2004). Lipton and his lab were able to use diffusion-tensor imaging. With this imaging technique they were able to find lower fractional anisotropy in the DLPFC for patients suffering from mTBI. This decreased fractional anisotropy is affiliated with lower performance rating on executive functioning testing (Lipton 2009). Similarly, Guay was able to discern a significant association between increased alpha brain waves in EEG analysis after sustaining multiple concussions (Guay 2018).

While these three studies were able to find significance in their research, they do not contain a large contribution to the effect size in regard to the larger population of studies. This preferred method within neuroimaging is not a very prevalent method compared to other mechanisms of study. Within this meta-analysis, only 2.9% of the studies performed neuroimaging as the mode of investigation. This percentage provides striking evidence that the array of research is not evenly distributed. With that being said, this perhaps suggests that there are other avenues that should be explored when researching the longevity of concussions.

The goal within this meta-analysis is to establish consistency with reference to the longevity of executive functioning deficits that arise post-mTBI. Additionally, this meta-analysis will present a detailed synopsis of the methods commonly utilized to assess cognitive functioning, specifically executive functioning, in individuals post-TBI. Executive functioning is by no means a definitive term. This term contains a vast number of meanings and interpretations within the neuroscience community. When trying to define executive functioning there are many avenues that can be used to distinguish this cognitive functioning domain. This term can be used when discussing attention, working memory, short term memory, long term memory, visual-spatial functioning, decision making, inhibition, etc. While each of these terms can be distinguished in some ways from one another, they all can be categorized as executive functioning of the frontal lobe. Furthermore, these intertwining networks of symptoms have shown the severity of this injury and more importantly the repercussions it may have. Due to the vastness of the term, it is hard to determine the significance and necessary emphasis this term should hold. When discerning the long-term deficiencies within mTBI injuries, this meta-analysis strives to better understand the effect executive functioning holds. Throughout the years, it has been found that individuals who suffer from mild-TBI in comparison to control groups exhibit long term deficits. With that being said, it is paramount to make this investigation and provide better education and understanding to this epidemic of TBI in order to diminish the prevalence of this injury.

Methods

Search strategy

The initial search strategy was very broad and began with the gathering of a plethora of scholarly articles from PUBMED and Google Scholar. The search was limited to papers discussing mild traumatic brain injuries and potential cognitive deficits. Keywords included “concussion”, “mild traumatic brain injury”, “head injury”, “executive functioning”, “deficits”, “neuropsychological assessments”, “self-report”, “neuroimaging” and several others. The reference sections of other meta-analysis or review articles were used to find alternative papers. This step was done to verify that all avenues were checked when building an abundance of papers. Papers ranged from 1985 to 2019, allowing for the discovery of any possible evolution on perceptions of mild traumatic brain injuries.

Selection criteria

The inclusion and exclusion criteria within this meta-analysis was created to eliminate confounding data that potentially could cause disorganized data, affect the effect size of the data and ultimately skew the data. For this meta-analysis, it was paramount for the studies to have reported a form of measure for central tendency, such as the means with coinciding measure of variance, such as standard deviation. The measure of central tendency and variance must have been recorded for the experimental group(s) (concussed) and control group (non-concussed). All studies that passed the selection criteria examined the comparison to negative control individuals, which was highly important. Each control presented with absolutely no history of concussion. These individuals were then compared to various participants that had suffered from at least a singular concussion.

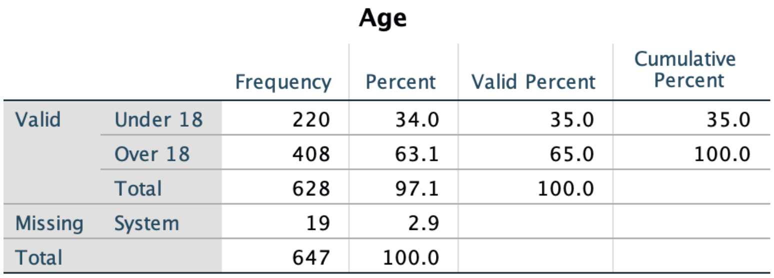
The criteria that were paramount for inclusion within the study were the means. It was not important whether the measure of central tendency was averages of rating scales, scores, time, accuracy, or even means for neuroimaging techniques. Several papers that had been collected prior to identifying inclusion and exclusion principles did not have a control group. This flaw in the various studies was a mode of exclusion for this meta-analysis. To measure the effect size, model estimates and significance values it is imperative to be comparing the concussed individuals to those who were the negative controls. This comparison allows for the computation of diverse statistical significance.

Several covariates were measured which included average age of individuals studied, number of concussions, testing technique and elapsed time since injury. These categories being used for this analysis would be analyzed both together and individually to see if there are significant differences in amount control and experimental groups. If the paper did not divulge any of the following covariates that was not sufficient evidence for exclusion from the meta-analysis. With the absence of any of the covariates from a study, the coder kept that cell left blank within the dataset.

Covariate frequency analysis

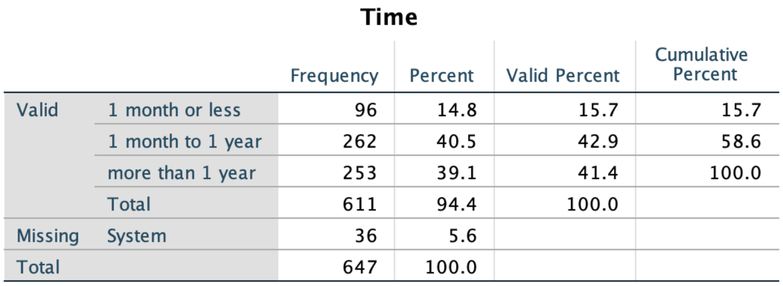
Once the data was gathered and cleaned within the dataset, the frequency within each covariates were gathered and further classified into the subcategories within each covariate. The valid and missing values were reported, along with the percentages in each category out of the entire dataset. There were approximately 600 studies that were examined within this meta-analysis. The frequencies fluctuated depending on the reporting rate within the individual studies. Within these frequency tables there were approximately 3-5% missing values within each of the tables. However within the “number concussions that have been suffered” covariate, there was roughly 25% of the data missing in the rate of studies reporting if the concussed individuals suffered from one or greater than one concussion (Table 2).

Table 2. Frequency and number of results included among each covariate. Provides the criteria within each subcategory (age, time since concussion, method of measuring deficits, and number of concussions.) Data presented shows frequency, percentage of dataset and the missing values within the dataset due to the study not reporting those variables.



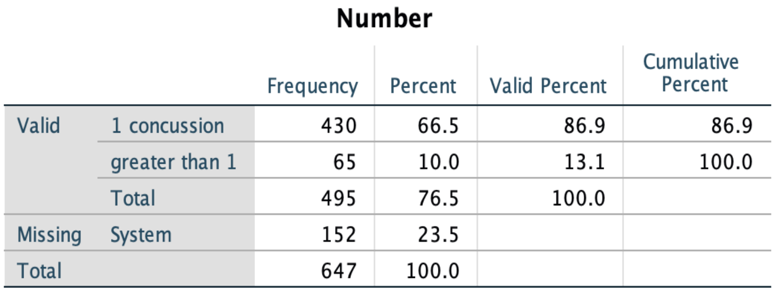
Age

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Under 18	220	34.0	35.0	35.0
	Over 18	408	63.1	65.0	100.0
	Total	628	97.1	100.0	
Missing	System	19	2.9		
Total		647	100.0		



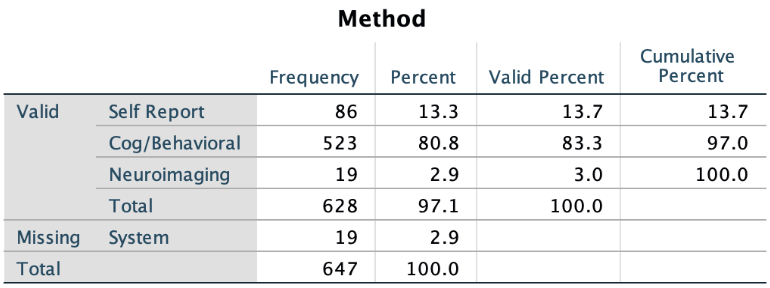
Time

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1 month or less	96	14.8	15.7	15.7
	1 month to 1 year	262	40.5	42.9	58.6
	more than 1 year	253	39.1	41.4	100.0
	Total	611	94.4	100.0	
Missing	System	36	5.6		
Total		647	100.0		



Number

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1 concussion	430	66.5	86.9	86.9
	greater than 1	65	10.0	13.1	100.0
	Total	495	76.5	100.0	
Missing	System	152	23.5		
Total		647	100.0		



Method

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Self Report	86	13.3	13.7	13.7
	Cog/Behavioral	523	80.8	83.3	97.0
	Neuroimaging	19	2.9	3.0	100.0
	Total	628	97.1	100.0	
Missing	System	19	2.9		
Total		647	100.0		

Data extraction and Statistical Analysis

Using OpenMetaAnalysis software, patented by Brown University, the mean differences, effect size, lower and upper bounds, and significance values were computed among the datasets. The model estimate was calculated for effect size to demonstrate how strong of a difference was between the following experimental and control groups. A negative effect size was indicative of the concussed group performing higher in whatever the variable measured. Contrastingly, a positive effect size represented a higher average among the control group for the technique being used. The "correct" or "expected" values for the effect size is relevant in association with the method and test that is being analyzed. When examining accuracy, it would be hypothesized that the control individuals would have a higher accuracy then those concussed, thereby, presenting a positive effect size. However, if the study is investigating reaction time, then you would expect the average time to be longer for concussed individuals then control, thereby making the effect size to be negative.

Further analysis of effect size, distributions, and frequencies were measured to decipher any further finds to help the inconsistencies and ambiguity that surround this research. Stem and whisker plot was used to conclude the distribution of strong, moderate and weak effect sizes among all the covariates. Additional histograms in affiliation with the stem and whisker plot were created to provide further visual representation of the frequencies within different effect size ranges. The Statistical Package for Social Science (SPSS) was used to do the following analysis.

Results

Overall model estimate and effect size strength

The overall analysis reveals a significant model estimate (ME) = -0.053, p=<.001. This finding represents an overall significant effect size across all tests and studies. A subjective interpretation of the strength of the effect size indicates that executive control is altered significantly in individuals with mTBI across multiple domains of testing and a variety of measures. The vast majority of findings (67%) show a moderate or strong effect size between mTBI patients and controls (Table 3). The various ranges for strength for effect size is comparing the means between the control and experimental groups, therefore, a strong to moderate strength shows a critical difference between groups being studied.

Table 3. Overall frequency and percentages within different effect size strengths among the entire dataset. Frequency= number of studies that fall within the predetermined ranges for varying strengths of effect size. Strong is above 0.8, moderate is between 0.3 and 0.8, weak is any effect size below 0.3. The percentages = (*n* within the specific strength range/ total *n* within the dataset).

Strength of Effect Size	**Strong** **range= |>0.8|**	**Moderate** **range= |0.3-0.8|**	**Weak/None** **range= |< 0.3|**
Frequency of studies (#n)	164	257	212
Percentage of entire dataset	26%	41%	33%

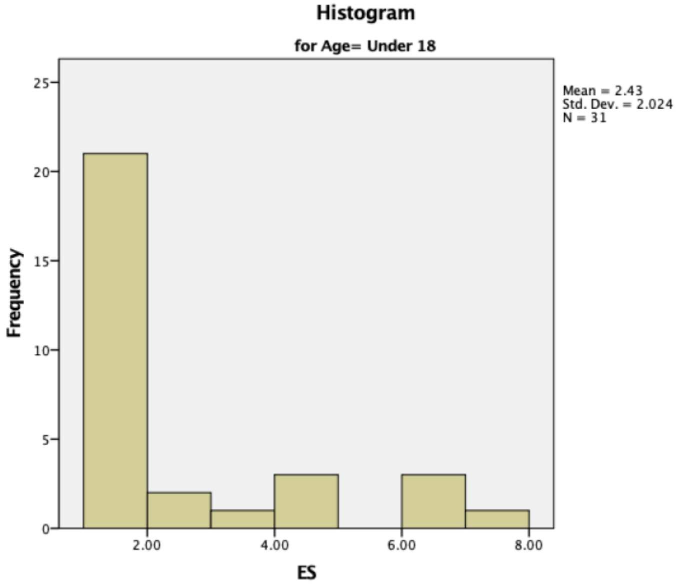
Effect Size Strength and Frequency by Age covariate

When delving into further analysis of covariate frequencies, there were striking percentages between and within strengths for the varying covariate subcategories. Within each covariate the majority of the studies provided data with strong to moderate effect size estimates. When examining both age groups, the majority of the data falls within the strong/moderate effect size. Within the entire dataset, the combination of both age groups displayed a substantial percentage (70%) with sizable effect estimates. Furthermore, even when looking between age groups, 64% of studies showed a considerable effect size when comparing frequency in the under 18 group. Similarly, the frequency of strong effect sizes, for the over 18 group, was about 70% of data within that age group (Table 4). The two additional histograms are added to contribute a visual representation of the dataset. This visual representation is able to show the spread of the data with an effect size greater than 0.1 (but in the figure 1 because the scale is ES x 10) (Figure 1).

Table 4. Frequency of effect size strength for the analysis of the Age covariate. Frequency is the number of studies that fall within the predetermined ranges for strengths of effect size, following the same criteria as Table 3. The frequency is then broken into the various subcategories within the age covariate, which is above or below 18 years old. The percentages are (*n* within the specific strength range/ total *n* within the dataset).

Strength of Effect Size	**Strong** **range= |>0.8|**		**Moderate** **range= |0.3-0.8|**		**Weak/None** **range= |< 0.3|**	
Age Category	Under 18	Above 18	Under 18	Above 18	Under 18	Above 18

Frequency of studies (#n)	43	112	62	121	60	83
Percentage within each age categories	26%	35%	38%	38%	36%	26%
Percentage of entire dataset	9%	23%	14%	25%	12%	17%



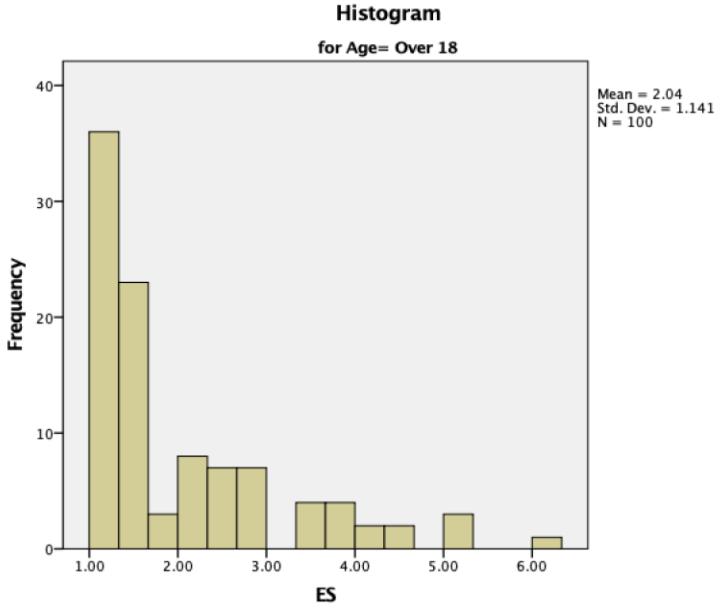


Figure 1. Histogram representation of effect size frequency ranging from 1.00 to 8.00 for the age covariate. The units for these graphs are computed effect sizes reported within the tables x10, therefore 0.8 in the table format is equivalent to 8 in the histogram (Table 2). There is a histogram for both under 18 (top) and over 18 (bottom). Due to showing close to no effect, data under 1 was excluded. The Under 18 histogram showed (M=2.43, SD=2.024, N= 31). The histogram for over 18, on the other hand displayed (M=2.04, SD=1.141, N=100).

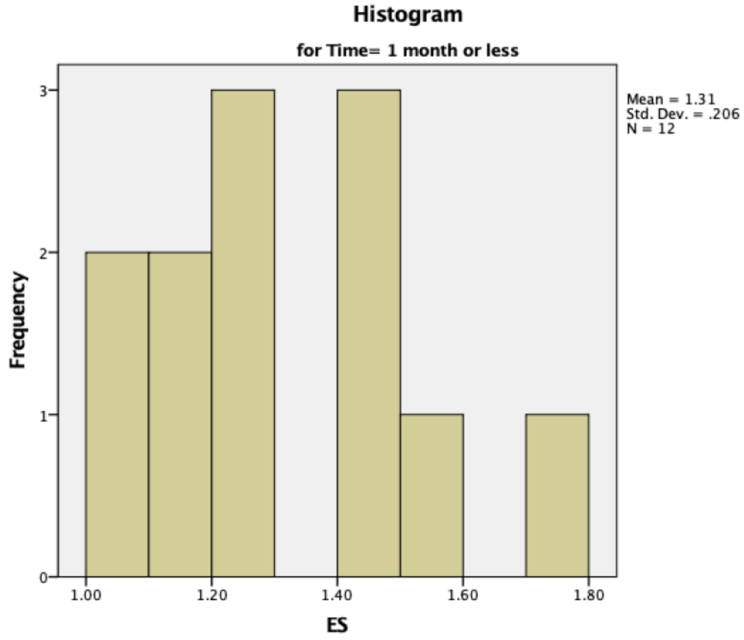
Effect Size Strength and Frequency by Time Since Injury Covariate

The majority of data showing strong effect estimates within and between covariates does not halt at age groups. The largest percentages of strong to moderate effect size is between 1 month to 1 year containing 78% of the data within its group and contribute 33% of the high effect size estimate to the entire data set (Table 5). The year or more category was closely behind in frequency within its group, however, showed a higher percentage of strong effect size among the entire data set. Within the longer time post-injury category, there was approximately 73% within its group with strong effect sizes and 34% between groups when comparing amongst the entire dataset for strength (Table 5). The subcategory for a month of less, while having a lower frequency of studies within the dataset, still the majority of the data fell within the strong/moderate effect (6.8%) (Table 5). The graphical depiction of this data establishes a rather right skewed spread for the subcategories of 1 month to 1 year and greater than a year (Figure 2). On the other hand the 1 month or less subcategory was able to provide a more normal distribution of effect sizes (Figure 2).

Table 5. Effect size frequencies for time since concussion covariate analysis. Frequency= n studies within predetermined ranges for varying strengths of effect size (table 3). The frequency

is then broken into the various subcategories within the time covariate. The subcategories are a month or less, a month to a year and greater than a year. The percentages are (*n* within the specific strength range/ total *n* within the dataset).

Strength of Effect Size	**Strong range= |>0.8|**			**Moderate range= |0.3-0.8|**			**Weak/None range= |< 0.3|**		
Time of concussion symptoms categories	1 month or less	1 month to a year	More than a year	1 month or less	1 month to a year	More than a year	1 month or less	1 month to a year	More than a year
Frequency of studies (#n)	15	72	77	18	94	82	18	48	77
Percentage within each time categories	28%	34%	35%	35%	44%	38%	35%	22%	35%
Percentage of entire dataset	3.1%	15%	16%	3.7%	19%	17%	3.7%	10%	16%



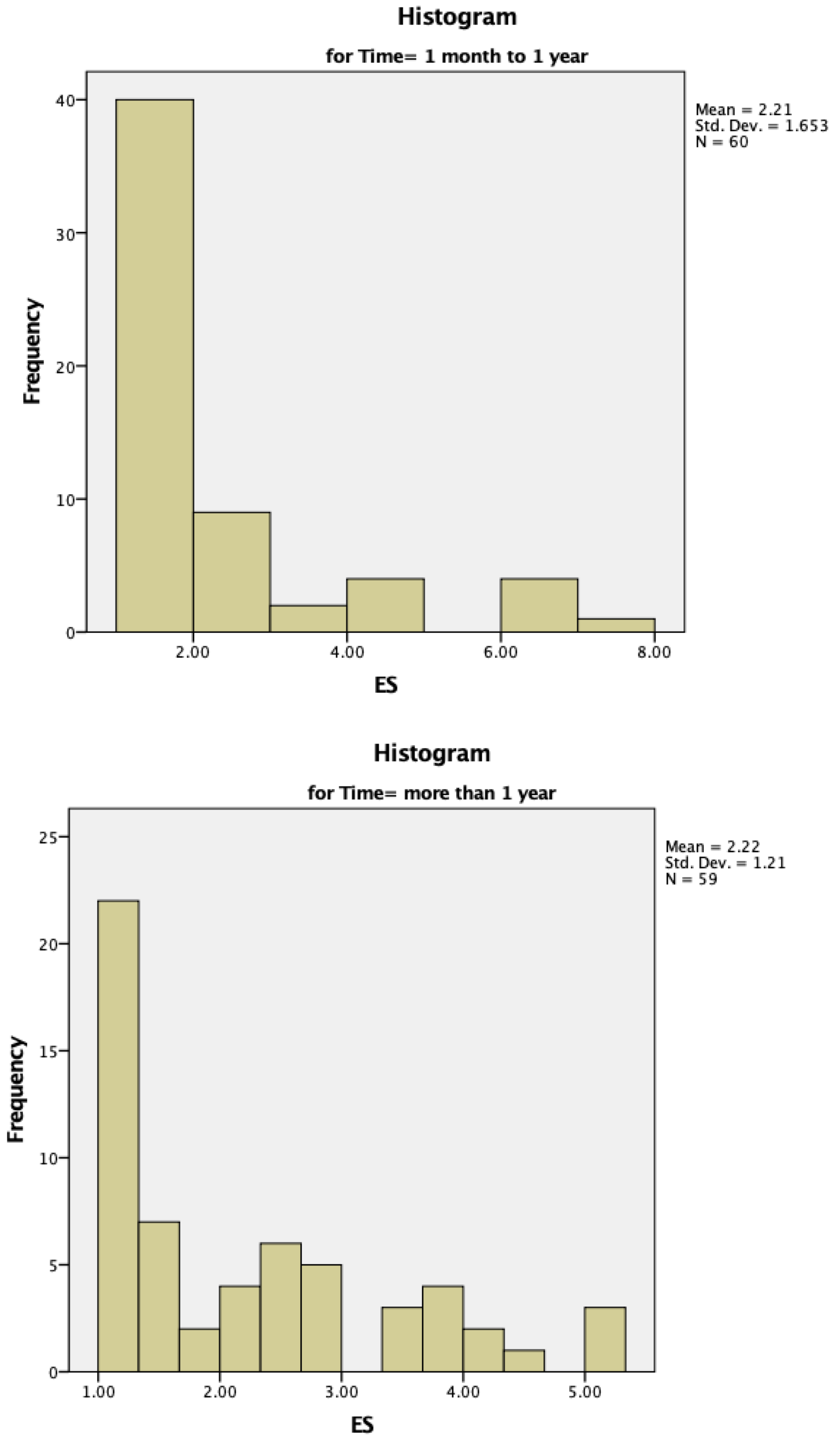


Figure 2. Visual representation of effect size frequency ranging from 1.00 to 8.00 for the time covariate. The units for these histograms are the effect sizes reported within the tables but x10, therefore 0.8 in the table format is equivalent to 8 in the histogram (table 2). There is a histogram

for 1 month or less (left) and 1 month to 1 year (right), over a year (bottom). Due to showing close to no effect, data under 1 was excluded. The month or less histogram revealed (M=1.31, SD=0.206, n=12). . The histogram for 1 month to 1 year presented the following data, (M=2.21, SD=1.652, n=60). The over a year histogram showed (M=2.22, SD=1.21, n=59).

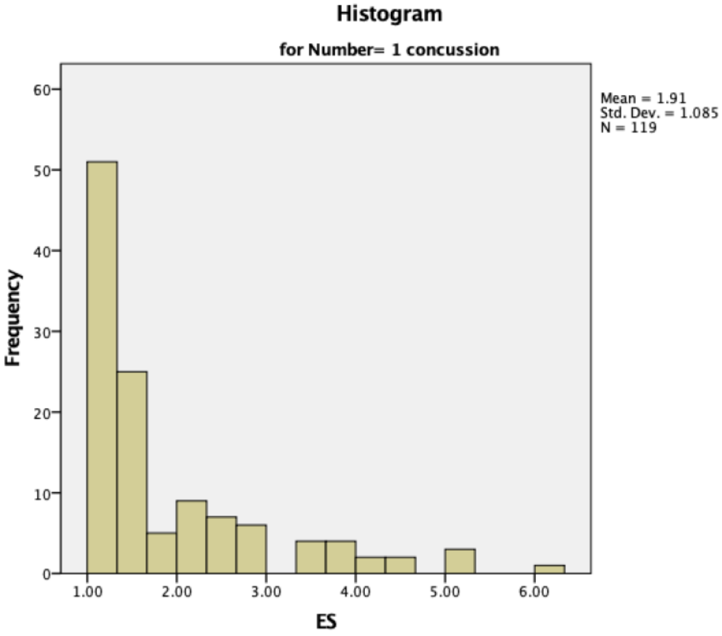
Effect Size Strength and Frequency for Number of Concussion Covariate

When investigating the frequency of data among the different sub-categorical variables within the number of concussion covariates, there was a substantial number of studies that examined individuals after suffering just a singular concussion (86%) versus the 14% that looked at participants that have suffered from multiple concussions. The group that suffered only one mTBI, the data was predominately strong to moderate effect size (75%). Contrastingly, for the studies that looked at individuals that suffered greater than 1 concussions, there was a greater percentage within the weak to no effect size as opposed to a large estimate of effect size (Table 6). This frequency distribution is thereby showing a larger population of studies are looking at deficits after a singular concussion instead of numerous concussions. However, further analysis was able to demonstrate a greater significant difference between the control and concussed group after suffering multiple concussions (Table 8). The visual representation of frequencies for the cohort of studies that measured participants that suffered from a singular concussion is clearly right skewed. However, the distribution of studies that investigated participants suffering from multiple concussions was more spread throughout 1-8 as the effect size.

Table 6. Frequency of effect size strength for number of concussion covariate analysis. Frequency = # of studies within the predetermined ranges for varying strengths of effect size

following the same criteria as previous tables. The frequency is broken into the various subcategories within the number covariate. The studies were coded as either investigating participants suffered from a singular concussion or from greater than 2 or more concussions. The percentages are (*n* within the specific strength range/ total *n* within the dataset).

Strength of Effect Size	**Strong range= |>0.8|**		**Moderate range= |0.3-0.8|**		**Weak/None range= |<0.3|**	
Number of concussion	One concussion	> 1 concussion	One concussion	> 1 concussion	One concussion	> 1 concussion
Frequency of studies (#n)	134	12	180	14	104	39
Percentage within each number category	32%	18%	43%	22%	25%	60%
Percentage of entire dataset	27.7%	2.5%	37%	2.8%	22%	8%



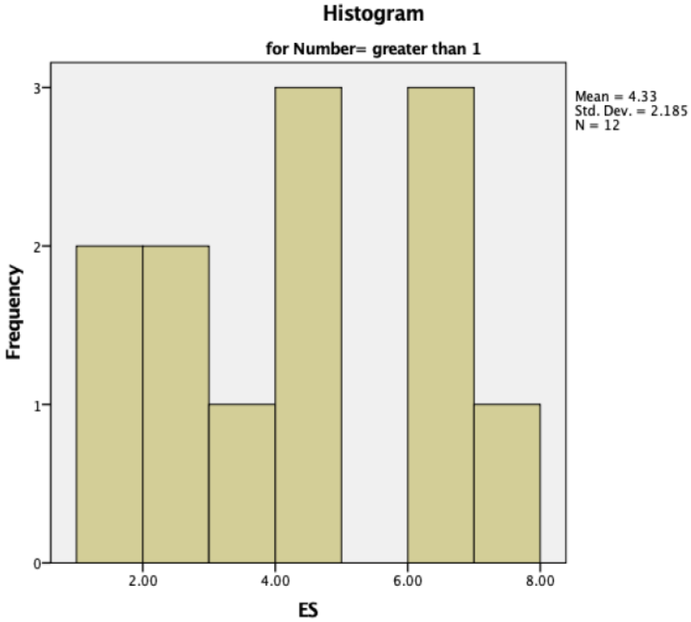


Figure 3. Histogram representation of effect size frequency ranging from 1.00 to 8.00 for number of concussion covariate. The units for these graphs are the effect sizes reported above but x10, therefore 0.8 in the table format is equivalent to 8 in the histogram (table 2). There are histograms for both 1 concussion (top) and greater than 1 (bottom). Due to showing close to no effect, data under 1 was excluded. The histogram for effect sizes of studies looking at deficits after suffering a singular concussion revealed (M=1.91, SD=1.085, n=119). The greater than one concussion histogram presented (M=4.33, SD=2.185, n=12).

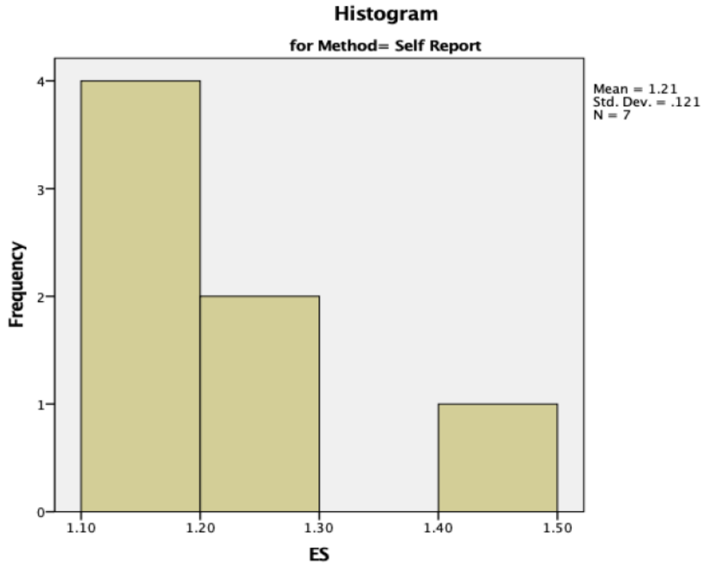
Effect Size Strength and Frequency by Method of testing Covariate

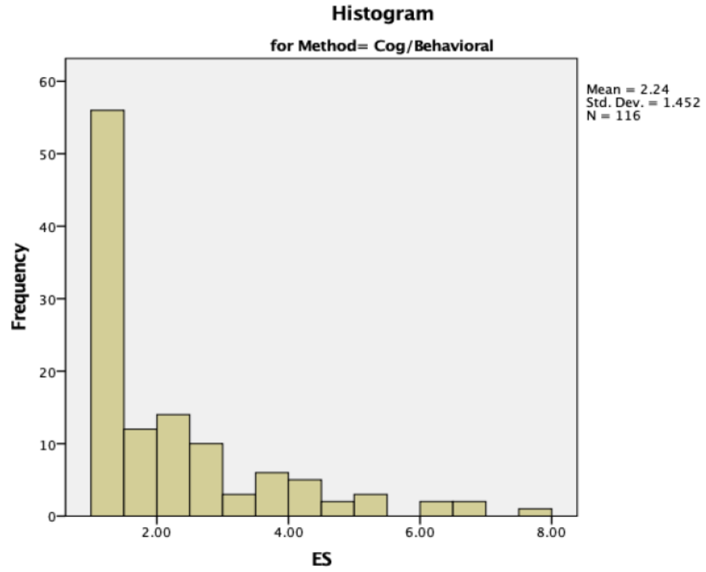
The following results verify the frequency and prevalence of cognitive/behavioral tests as being the predominant mode of testing for examining the deficits post-injury. Approximately, 80% of the studies that were examined used neuropsychological evaluations as the mode of testing, while the remaining studies used self-report forms and neuroimaging. Similar to the previous covariates, the frequency of studies with a strong to moderate effect size is noticeably greater than weak/no effect size (Table 7). When comparing the strong/moderate percentages to weak percentages for each method, which included self-report, neuropsychological, and neuroimaging, the percentages within the higher effect size were 75%, 70% and 80% respectively (Table 7). Regardless of the method the data demonstrate that you can show a high model estimate, however, shows little to no significant difference, which is subjectively seen within the percentage and frequency below. The visual depiction of the frequency table provides a clearer spread of data and enhanced visualization of the different ranges of strength for effect size. The spread for both the self-report and neuroimaging had a small spread of data. This is primarily due to the limited sample size for those two methods of testing. On the other hand, the cognitive and behavioral tests show a much larger range of data because of the more robust number of studies that were coded.

Table 7. Frequency of effect size strength with covariate analysis for methods of testing. Frequency= number of studies that fall within the predetermined ranges for varying strengths of effect size following the same criteria as Table 3. The frequency is then broken into the various subcategories and within the method covariate that consists of self-report measures, cognitive/behavioral tests and neuroimaging. The percentages are (*n* within the specific strength range/ total *n* within the dataset).

Strength of Effect Size	**Strong range= |>0.8|**			**Moderate range= |0.3-0.8|**			**Weak/None range= |< 0.3|**		
Method of testing	Self-report	Cog/ Behavioral	Neuro-imaging	Self-report	Cog/ Behavioral	Neuro-imaging	Self-report	Cog/ Behavioral	Neuro-imaging

Frequency of studies (#n)	8	127	11	29	161	4	12	128	3
Percentage within each method category	16%	31%	61%	59%	39%	22%	24%	31%	16%
Percentage of entire dataset	1.7%	26%	2.2%	6%	33%	0.8%	2.5%	27%	0.6%





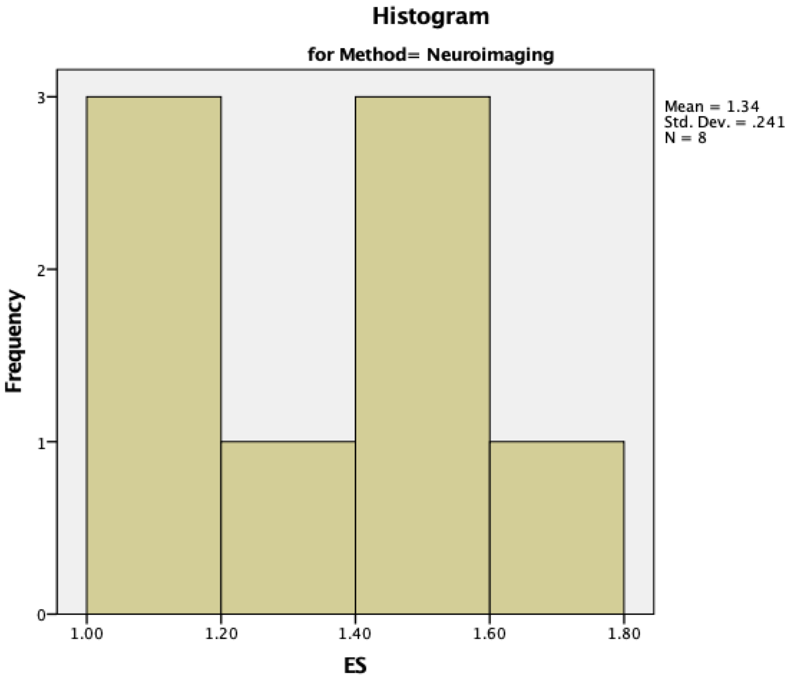


Figure 4. Histogram representation of effect size frequency ranging from 1.00 to 8.00 for the methods covariate. The units for these graphs are the effect sizes reported above but x10, therefore 0.8 in the table format is equivalent to 8 in the histogram (table 2). There is a histogram for self-report questionnaires (left), cognitive and behavioral tests (right) and neuroimaging techniques (bottom). Due to showing close to no effect, data under 1 was excluded. The self-report questionnaire histogram had an average of 1.21 effect size and included 7 studies within the graph (M=1.21, SD=0.121, n=7). The histogram for cognitive and behavioral tests, had a mean effect size of 2.24 for approximately 116 studies (M=2.24, SD=1.452, n=116). The neuroimaging technique histogram showed a mean of 1.34 for the 8 studies that were included (M=2.22, SD=1.21, n=59).

Model estimate and significance based on covariates

In conjunction with the results that the majority of the studies demonstrated strong to moderate effect sizes among each covariates, the dataset also confirmed a significant differences between the experimental (concussed) group and control groups when further classified into sub-categorical covariates (Table 8). Regardless of the age of the participants there was a very significant estimation difference between variable groups (*under 18:* ME= -0.067, p <0.001; *above 18*: ME=-0.087, p= 0.001) (Table 8). These results are thereby indicating that when classifying between those two age groups there are still significant differences being found within literature.

Researchers tend to spend a lot of time distinguishing the time since their injury. The duration of these deficits is still ambiguous, the analysis of these hundreds of studies revealed a significant difference between groups at less than 1 month, 1 month to 1 year post injury (ME=-0.078, p=0.01; ME= -0.175, p< 0.001 respectively) (Table 8). However, there was no substantial statistical difference between the control and concussed groups for greater than 1 year post injury studies (ME=0.051, p=0.106) (Table 8).

This time interval is paramount when understanding the proper treatment regimen, therefore, this meta-analytical approach allows the comparison of experimental and control groups between hundreds of studies. Throughout these hundreds of studies each team of researchers chose what they believed would be the most beneficial method for demonstrating the long term executive functioning deficits after a mTBI. These methods fell within the following categories, self-report, neuropsychological evaluations (cog/behavioral tests) and functional neuroimaging, all of which exhibited significance except for the neuroimaging techniques. The largest frequency among the dataset was neuropsychological evaluations (n= 416), demonstrating very significant findings (ME= -0.069, p<0.001) (Table 8). Following the largest frequency of neuropsychological evaluations, self-report forms (n=49) similarly showed high significance (ME= -0.469, p<0.001) (Table 8). Divergently, there was no significance among groups when the studies decided to use neuroimaging (n=18) as their method of testing for executive functioning deficits (ME= -0.019, p=0.298) (Table 8).

The final covariate that was investigated and coded within meta-analysis was the distinction between studies that looked at a singular mTBI or greater than one concussions. Interestingly, there were little frequency of studies that had strong to moderate effect size within the greater than one concussion group, nevertheless there was a significant difference between the concussed and non-concussed groups (ME=-0.125, p<0.001) (Table 8).

Table 8: Model estimate and corresponding p-value for each covariate subcategories. Model estimates are the estimated difference between the means between groups. The p-value is set at a significance value of less than 0.05.

Age		**Model estimate**	**p-value** Significance= p<0.05
	Under 18	-0.067	<0.001
	Above 18	-0.087	0.001
Times since concussion	**1 month or less**	-0.078	0.01
	1 month to a year	-0.175	<0.001
	More than a year	0.051	0.106

Method of Testing	**Self- report**	-0.469	<0.001
	Cog/ Behavioral	-0.069	<0.001
	Neuroimaging	-0.019	0.298
Number of concussion	**One concussion**	-0.029	0.189
	> 1 concussion	-0.125	<0.001

Discussion/Conclusion

This meta-analysis sought to provide substantial evidence to the severity and longevity of mTBI. Results indicate strong effect size and significant findings amongst literature, thereby, indicating the need to implement better education and understanding of this epidemic of mTBI. With better comprehension of this injury we as a scientific community can hopefully diminish the prevalence of this injury. The significance across most covariates is able to demonstrate comprehensive analysis. The documentation of significance and strength of findings over hundreds of studies, rather than simply a singular study is in itself the main advantage to meta-analysis. The overall model estimate including all the studies with no exclusion for covariates was able to show an overriding significance between groups ($p<0.001$). The significance within this dataset strengthens the previous researched studies that have found longevity and severity at a variety of ages through a plethora of tests after suffering from at least a singular concussion. By cohesively analyzing an abundance of data, the validity of these deficits can be strengthened and therefore be more applicable to the larger population.

Unfortunately singular studies do not carry the same validity. If scientists were to pick from the pool of data, several independent studies, they would most likely find variable findings.

When comparing two studies that did the same digit span test, one found significance while the other found an association but no significance between control and concussed (experimental) groups (Wall et al. 2006; Vasquez et al 2018). Interestingly, each had the same coding for the various covariates besides the time since the concussion. Wall's lab looked at the demographic that was above 18, suffered one concussion, but was from a month to a year since the injury. On the other hand, Vasquez looked at the same demographic yet the experimental group had suffered from their injuries greater than a year ago. Now, the ambiguity in these results is that one would assume that the study that looked at the testing early post-injury was significant, nevertheless that was not the case (Wall et al. 2006; Vasquez et al 2018). Vasquez's team found significance within their study, which is further emphasized by a strong effect size for that study (ES= 2.33) (Vasquez et al 2018). Wall and his team contrastingly found little significance and that if further amplified by the very weak effect size (ES=.12) (Wall et al. 2006). Despite the fact that these two singular studies provide ambiguity to our understanding, this meta-analysis was able to weight these effect sizes and find a significance that is applicable to the population. Increasing the sample size within the meta-analytical methods creates more strength for effect size to be relevant to our overall population.

When interpreting what level of understanding the scientific community currently has regarding mTBI, it is paramount to look at the various covariates that have been analyzed within this meta-analysis. Each of the covariates investigated are an important puzzle piece for grappling with this convoluted injury. These covariates present stronger insight to this investigation. When trying to further understand the significance further down the line of this injury, age of the incident is an extremely influential variable to investigate. Per the CDC, the rate of adolescents experiencing concussions has only increased over the years (DePadilla 2017).

Researchers have found through various methods that children who have suffered from concussion have experienced significant deficits in comparison to controls that are within the same age group. Investigators have seen severe deficits within visual and working memory, attention and even neuroelectric alterations within the brain (Mangoet et al. 2002, Moore et al. 2016). These deficiencies are only several of the executive functioning effects that come from suffering from a brain injury at a young age. Scientists have been able to discern that the earlier the injury occurs the increased likelihood of deficits behaviorally and neurologically (Moore et. al 2016). These significant discoveries found previously can be reinforced by the findings within this meta-analysis. The significance between control and experimental groups among the entire meta-analysis, as well as 64% showing of the studies showing a considerably strong effect size highlights how the younger population is at risk when suffering from a concussion. There is an urgency within these rates and findings due to the adolescent brains still needing to complete maturation. During the brain development there is not only neuronal growth and plasticity occurring but accompanied continuous behavioral changes. The behavioral growth consists of increasing concentration, establishing memory pathways, problem solving and other executive functioning skills. The complex biological processes and neurological pathways have been seen to be altered after a child endures a mTBI. This should be a wakeup call to the scientific community to continue the growth of organizations that raise awareness of the injury, increased education of the topic, and additional research in the future. The incidences of concussions are not just important among younger children. The covariate of time has also been seen as an extremely important variable when building a more comprehensive analysis for the longevity of concussions.

The long-term consequences of mTBIs are a continuous avenue of study that has produced serious inquiries on the longevity of the injury. Many scientists have found clear differential results in comparison to controls when it is less than a month post-injury. However, after a couple months post-concussion the findings can be ambiguous on the longevity of the injury.

This meta-analysis was able to amplify the well understood deficits short term through significant findings between groups at the lowest time subcategory (ME=-0.078, p=0.01, Table 8). Interestingly, this model was able to find additional significance within the literature that investigated injury from 1 month to 1 year post injury (ME= -0.175, p< 0.001) (Table 8). By providing this significance, it strengthens the argument that there is possibly long-lasting inadequacy cognitively. However, our model was unable to provide substantial statistical divergence for literature that studied individuals with greater than 1 year post injury (ME=0.051, p=0.106) (Table 8). The literature that studied participants 1 year or greater post injury was approximately 40% (n=253) of the dataset (Table 1). There were several studies that presented very strong effect sizes that ranged from 1-5, which is well above the 0.8 threshold for a strong effect size. These studies were able to display severe deficits among individuals that have suffered from TBIs. These studies used tests ranging from event related potentials to numerous neuropsychological evaluations (Perlstein et al. 2005; Valet et al. 2007). Nevertheless there are still studies that fail to find statistical differences between groups (Ewing-Cobbs et al. 2004). While this may be a relatively large proportion of the meta-analysis dataset, it provides insight into the avenues that need to be explored further in order to improve knowledge on this injury.

While it may seem like common sense that the more concussion one endures the greater the severity and longevity of deficits. This is not entirely the case, similar to the other covariates within this dataset, there is continually indefiniteness within the scientific community for effects after suffering greater than one mTBI. The deficits after suffering greater than a singular concussion is not highly researched and understood. In this dataset alone, the studies that looked at participants who have suffered greater than one mTBI is approximately only 10% and the remaining 90% which were studies looking at effects after a singular mTBI injury or was not distinguishable when coding. However, regardless of the small sample size, the studies included showed a large model estimate and very significant difference between groups being examined (ME= -0.469, p<0.001 Table 8). Therefore, these compelling results present further evidence to push for this covariate to be studied to a greater capacity. Jacklyn Ford was able to study within her lab both behavioral effects and neurological recruitment deficits among groups that suffered anywhere between one to three concussions. Intriguingly she was able to find decreased ability in recruitment of brain regions during certain tasks as the number of concussions increased. Unfortunately she was unable to obtain significance with neuropsychological testing (Ford et. al. 2013). The significance in deficits among those who have suffered from greater than one concussion is present, however, is inconclusive between different methods. These contradictions demonstrate the need for further research after suffering from multiple concussions as well as the subsequent covariates, such as methods of testing.

The techniques used to test cognitive function post-concussion are very unproportionate and inequivalent in regard to the utility within the scientific community. In this meta-analysis alone, 80% was cognitive and behavioral tests, while there was only 13% for self-report measures and 3% for neuroimaging techniques (Table 2). As discussed previously, there are several advantages and disadvantages within each method. Due to the high utility of cognitive and behavioral tests it is little surprise the majority of the studies had strong effect sizes and the model estimate for the entire dataset was very significant (p<0.001, Table 8). This result thereby proves the continuous practicality of these wide variety of tests. Neuropsychological tests include, no-go test, RBANs, WAIS, digit span, or the Stroop Test, all of which are able to test diverse cognitive measures like immediate memory, working memory, verbal fluency, inhibition, and many testing attentional deficits. Regardless of the small proportion of studies that used self-report forms there was still significance that was found between controls and concussed when analyzing the entire dataset (p<0.001, Table 8). The Behavior Rating Inventory of Executive Function (BRIEF) is a common self-report survey used within the study of cognitive deficits after a brain injury. Within these questionnaires, participants who have suffered a mTBI generally reported greater deficits cognitively, behaviorally and perhaps just throughout day-to-day life (Mangoet et al. 2002; Krivitzky 2011). This is a very bias way of analyzing deficiencies within individuals after injuries, but is a great preliminary method to see how the individuals perceive the inadequacy of performance for certain tasks. A common mechanism of eliminating the biases from understanding these deficits is performing behavioral testing, as well as neuroimaging techniques. Within the sample size that used neuroimaging there was a large percentage that obtained strong effect sizes (80%); however, the strong effect sizes were dampened by the lack of studies. The low sample size caused the effect estimate to be weakened, thereby causing insignificant findings between groups (p=0.298, Table 8).

Looking into the future of this field it will be interesting to see if the utilization of neuroimaging will increase. This increase could potentially create a clearer picture of the deep seeded neuronal deficiencies resulting from brain injuries. Our reliance on cognitive measures needs to become more evenly distributed in order to provide a cohesive meaning of the short- and long-term effects of brain injuries. The use of functional neuroimaging could reshape our knowledge of mTBI. Using functionally neuroimaging in conjunction with neuropsychological evaluations will allow for the investigation of certain regions of the brain and how alterations at a structural, cellular and molecular level are influencing the behavioral and developmental aspects of life. This connection will be important for the future of brain injury research.

Despite the fact that this meta-analysis is able to exhibit various significant findings that are able to strengthen the individual literature, there are still limitations within the meta-analysis. As Belanger and Vanderploeg reported in their meta-analysis on sports related concussions, there are several inherent limitations to meta-analysis (Belanger & Vanderploeg 2005). Within the study a significant limitation is the inconsistencies that could occur when coding. As there are several people within this lab, there are various people coding the articles. Each lab member has varying experience levels reading scientific papers and an overall inconsistent level of knowledge on brain injuries. The potential for error within coding could have occurred such as the knowledge between methods of testing. However there can also be simply systematic error when inputting the data or surveying papers, which could potentially skew the data to a potential lack or presence of significance. Further skewing of data could also have occurred due to the smaller sample size of studies. A greater cohort of studies would provide greater significance and cohesiveness to this meta-analysis

Despite these limitations, this meta-analysis was still able to provide significance not only within the entire data but in the majority of the sub-categorical covariates that were being analyzed. With these results, it is clear the meta-analysis is a strong way of presenting the effect size within a population for two distinct groups. Additionally, it was made clear the urgency of this injury. The significance in deficits for younger children, greater than 1 concussion and up to a year after the injury are key components that must be studied further. By being able to understand the injury it creates the ability to increase awareness and education on the issue. The finding may also lead to improvement in treatment regimens, organizations and initiatives that can help this epidemic of mTBIs.

Acknowledgements

I would like to thank Dr. Joel Bish and all members of the concussion lab for their assistance with coding and statistical analysis. I would also like to thank the Neuroscience and Psychology departments at Ursinus College for providing me this opportunity to do research. Special thanks to Statistical Package for Social Science (SPSS) and OpenMetaAnalysis software for the ability to use these programs for statistical analysis.

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