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The Effects of Caffeine on Reaction Time of Two Neurocognitive Tests

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TWO NEUROCOGNITIVE TESTS

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44 Pages

Context: A concussion is defined as a traumatically induced transient disturbance of the brain caused by a biomechanical force. These problematic injuries can prevent athletes from participating in physical activity for a number of days, weeks, or even months. Caffeine is known for improving mental alertness in everyday tasks and is found in many popular drinks such as, coffee, tea, energy shots, and even soda. Due to its increase in memory, mental alertness, and concentration, caffeine could potentially be utilized to improve the outcomes of post-concussion neurocognitive testing. This improvement would allow athletes to return to play before they have returned to full health, thus potentially setting them up for further brain trauma. **Objective:** To evaluate caffeine's effect on reaction time (RT) when measured with two neurocognitive evaluation tools. **Design:** Cross-sectional Observation. **Setting:** Athletic Training Laboratory. **Patients or Other Participants:** Eighteen (14 male and 4 female) (Age = 21.7 ± 1.4 years, Height = 175.0 ± 9.1 cm, Weight = 75.6 ± 12.5 kg) healthy college students participated in the current study. They were excluded if they had a history of high blood pressure, diagnosed heart condition, neurocognitive disorder or clinically diagnosed mental illness, more than one concussion in their lifetime or one within the last year, caffeine sensitivity, currently taking any prescribed medications, except birth control, ingest more than 500mg of caffeine daily or have been exposed to Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) or Kind-Devick tests within the last year. **Interventions:** Participants were randomly assigned into either a caffeine or placebo group. Following ingestion of the intervention, participants waited 45 minutes to begin their first assessment, either ImPACT or the King-Devick (KD) Test. Immediately following the first assessment, participants were evaluated using the other neurocognitive tool. Follow-up testing was conducted one week later under the opposite intervention. The testing order remained the same between the two testing sessions. **Main Outcome Measures:** The reaction time composite score produced by ImPACT and the overall King-Devick time were recorded and evaluated for initial testing and the follow-up appointment. These domains were compared to evaluate caffeine's effect on reaction time compared to the placebo intervention. Scores were also evaluated for each testing session regardless of the intervention. This evaluation will indicate if there is a practice effect overtime. **Results:** A significant improvement was noted in the ImPACT RT score following ingestion of the stimulant (0.53 ± 0.05 seconds) compared to the placebo substance (0.56 ± 0.07 seconds, P=.007). The KD test resulted in a significant decrease in overall time between testing session 1 and testing session 2, suggesting a practice effect (38.2 ± 5.6 seconds, 35.5 ± 5 seconds, P= ≤ 0.001). **Conclusions:** Participants of the current study were able to identify a computerized stimuli 0.03 seconds faster following ingestion of caffeine. Although ImPACTs RT reliable change

index score of 0.06 seconds was not met, the improvement following caffeine for the current study is worth noting. The proposed clinical question still remains, should medical professionals inquire about caffeine intake prior to neurocognitive testing, to minimize possible threats to the evaluation process.

KEYWORDS: Caffeine, Concussion, Neurocognitive Testing, Reaction Time

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CHAPTER I

THE PROBLEM AND ITS BACKGROUND

Introduction

It is estimated that 1.6- 3.8 million sport-related concussions occur each year in the United States.[1] A concussion is defined as a traumatically induced transient disturbance of the brain caused by a biomechanical force.[2,3] These problematic injuries can prevent athletes from participating in physical activity for a number of days, weeks, or even months. It has been shown that high school athletes only report head trauma roughly 50% of the time,[4] resulting in many individuals compromising their health to not miss competition.

Current consensus statements recommend that the management of sport-related concussions be based on a multifaceted approach that includes symptom inventories, balance assessments, and neurocognitive evaulations.[5-7] Of the three aspects for managing concussions, neurocognitive evaluation provides the greatest amount of objective clinical information.[8] The most widely used computerized neurocognitive assessment in North America is the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) tool which has shown to be a reliable[9,10] and valid[11-13] means for evaluating sport-related concussion. ImPACT consists of 3 main sections demographics, post-concussion symptoms and neurocognitive test modules.[14] The testing modules evaluate the athlete in five mental aspects that are believed to be diminished with the presence of a concussion; concentration, attention, memory, visual motor speed, and reaction time (RT).[14] As stated earlier, some athletes will do what they can to speed up post-concussion return to play. This could range from athletes lying about post-concussion symptoms, to theoretically attempting in modify their mental state with caffeine prior to taking a computerized neurocognitive test.

Recently, another post-concussive neurocognitive test has been developed that provides clinicians with an easily administered option, yielding in a prompt insight to the presence of a concussion. The King-Devick (KD) test involves reading aloud a series of random single digit numbers from left to right on three different testing cards.[15] The participant is assessed based on the total time it takes the person to read all three testing cards. The post-concussive results are compared back to a previously taken baseline test to determine if any deficits are present. Poor King-Devick test results have been associated with impairments in reaction time and visual motor speed when compared to ImPACT.[16] Inversely, it has been shown that improvements in concussion status are correlated to positive results on King-Devick and ImPACT.[17] The current test requires rapid eye movement, proper language function and sustainable attention to complete, all of which tend to be difficult to do in the presence of a concussion.[18-22] Theoretically, the results of this test could be manipulated by improving attention and motor processing speed with the presence of caffeine.

Caffeine is known for improving mental alertness in everyday tasks[23] and is found in many popular drinks such as, coffee, tea, energy shots, and even soda. Caffeine increases cortical activation, information intake and improves motor processing via central and/or peripheral mechanisms.[24] These perceived improvements are due to the binding effects of caffeine to adenosine receptors, thus disinhibiting neuronal firing throughout the brain.[25,26] Improvements on physical performance, such as reaction time in youth soccer athletes during reactive agility tests,[27] as well as improvements in early sprint performance over a 30 meter distance[28] have been evaluated after ingesting caffeine. Reaction time improvements have also been present during repeated taekwondo kicking activities in healthy individuals.[29] Other studies have shown increases in mental factors such as sustained attention, cognitive effort and reaction time following the administration of caffeine. [30-32] An everyday task such as driving performance (speed variability and weaving of the car) was significantly improved following caffeine consumption.[33] Due to this increase in memory, mental alertness, and concentration, caffeine could potentially be utilized to improve the outcomes of post-concussion neurocognitive testing. This improvement would allow athletes to return to play before they have returned to full health, thus potentially setting them up for further brain trauma.

Powers[34] looked at the effects of a caffeinated pre-workout supplement (Jacked 3D) on ImPACT scores in all 6 composite categories. There were slight improvements in reaction time, visual processing speed and memory. However, the author could not determine if the improvements were from the caffeine or other stimulating ingredients in the supplement. It was also noted that the supplement was a powder, making it impossible to ensure every participant received the same amount of stimulating ingredients.[34] Energy shots, which are popular among college-aged students and athletes, provide a consistent amount of caffeine and other ingredients during consumption. A popular energy shot, 5-hour energy®, combines 30mg of Niacin, 40mg of vitamin B6, 400mcg of folic acid, 500mcg of B12, 18mg of sodium, 200mg of caffeine and 1870mg of an energy blend into every 1.93 fl. oz container.[35]

Currently, there has been no research examining the effects of an energy shot prior to ImPACT or King-Devick neurocognitive tests. Therefore, the purpose of this study was to determine the effects of an energy shot on reaction time when measured using ImPACT and King-Devick tests on healthy college aged students, as well as assess learning effects from the two sessions. We hypothesized that caffeine would improve reaction time on both neurocognitive assessments.

CHAPTER II

REVIEW OF RELATED LITERATURE

Anatomy

The brain is one of the most important organs in the human body and yet the least understood.[36] Injuries to the brain are something that can be temporarily or in severe cases permanently crippling. Due to its complex make up, it is difficult to know exactly what portion of the brain is damaged following injury. A fleet of tests can be done with the intent to narrow down the anatomical damage as well as the extent of this damage.

Cranium

The brain is almost fully enclosed by bone, which is often referred to as the cranium or simply the skull.[36] The skull is considered a single structure that is ridged in adults and pliable in children thus making children more susceptible to injury.[36] Due to its rounded shape, the skull is designed to deflect impact to protect its underlying organ.[36] Often forgot about, the skin acts as another protective device, increasing the craniums ability to absorb and redirect forces.[36]

Brain

The cerebrum is the largest portion of the brain and is divided into two hemispheres.[36] These hemispheres are then divided into the frontal, parietal, temporal and occipital lobes based on the overlying bones.[36] The cerebrum has the important job of controlling primary motor functions such as gross muscle contractions and the coordination of specific muscle contraction sequences.[36] This large portion of the brain is also in charge of sensory information such as temperature, touch, pain, pressure and proprioception.[36] Damage to one hemisphere of the cerebrum will affect the contralateral aspect of the body due to its cross-over responsibilities.[36]

The cerebellum's responsibilities are at more of a refined and particular level. The sensory information related to balance and coordination are often passed from the cerebrum to the cerebellum.[36] This sensory information allows the cerebellum to modify motions to ensure they are smooth and fluid in nature, such as picking up a glass of water.[36] The cerebellum may be damaged from a direct blow to the posterior skull, along with acceleration and deceleration mechanisms.[36] Damage to this aspect of the brain can sometimes be easily spotted due to ones uncoordinated, segmental, robot-like movements.[36]

The diencephalon is the processing center for conscious and unconscious movements and is typically broken into the thalamus, hypothalamus and epithalamus.[36] The thalamus evaluates the ascending sensory information and disperses it to the appropriate aspect of the brain.[36] The hypothalamus is responsible for regulating the body's hormone balance along with the sympathetic and parasympathetic nervous systems.[36]

The link between the brain and the spinal cord is known as the brain stem. The brain stem is broken down into the medulla and pons, with the pons directly connecting to the cerebellum.[36] The brain stem is in charge of several involuntary actions such as breathing, coughing and vomiting.[36]

Meninges

The brain and spinal cord are separated from their outer lying surfaces by three barriers known as meninges.[36] These meninges are primarily responsible for support and protection along with housing the arteries and veins needed to support the blood supply to the brain.[36] The outermost layer, often referred to as the dura mater, acts as a periosteum to the skull and provides the bones with their blood supply.[36] The arachnoid mater is located below the dura mater and is more resilient to trauma.[36] The arachnoid mater is separated from the other meninges by two spaces, the subdural and subarachnoid which are located above and below respectively.[36] The subarachnoid space is filled with cerebrospinal fluid (CSF), which provides an extra layer of protection to the underlying brain.[36] The CSF allows the brain to have a "floating" effect, which will act as a buffer for small repetitive trauma such as running.[36] Although this effect provides protection to smaller forces, it is ineffective to large blows and may allow the brain to contact the inner wall of the skull.[36]

Cranial Nerves

Located in the brain are twelve cranial nerves which are in charge of transmitting both sensory and motor impulses.[36] The ganglia of the sensory nerves are located outside of the central nervous system and can easily be damaged from increased pressure in the skull.[36] Damage to these aspects of the sensory nerves could be responsible for changes in vision, taste, and smell.[36] The ganglia of the motor aspects of each nerve is located inside the central nervous system and are rarely damaged.[36] Damage to these aspects could lead to the loss of eye function, facial movements, and the process of swallowing.[36] Following brain trauma, every cranial nerve should be assessed to ensure there is no underlying damage. The order of the cranial nerves are as follows: Olfactory, Optic, Oculomotor, Trochlear, Trigeminal, Abducens, Facial, Vestibulocochlear, Glossopharyngeal, Vagus, Accessory, and Hypoglossal.[36]

Trauma

In extreme cases of trauma, vessels in the brain may rupture causing the release of blood known as an intracranial hematoma.[36] This blood can place significant pressure on the brain, causing damage to several aspects and may even cut off oxygen needed for survival.[36] There are two hematomas that could possibly occur each of which with its own distinct set of traits. An epidural hematoma is often an arterial bleed located between the dura mater and skull.[36] This hematoma usually forms quickly with symptoms occurring within hours of the direct trauma which typically is from a blow to the head that jars the brain.[36] A subdural hematoma on the other hand, does not show symptoms for a number of hours, days or even weeks and is responsible for the majority of athletic-related head trauma.[36] In opposition to an epidural hematoma, a subdural bleed occurs from venous drainage thus causing it to be significantly slower than the previously stated arterial bleed.[36] Education of parents, siblings and friends is important in recognizing these serious bleeds, as any abnormal or worsening of symptoms signifies an immediate referral to the emergency room.[36]

Concussion

Sport-related concussions occur 1.6 to 3.8 million times annually in the U.S.[1] and account for 5-9% of all sport-related injuries.[37,38] Despite such a high number occurring annually it has been demonstrated in previous studies that athletes, parents, and coaches lack the knowledge needed to make informed decisions about concussions.[39-41] This lack of knowledge may lead to future complications that could be detrimental to an athlete's health. The care of athletes with sport-related concussions should be performed by a healthcare professional with specific training and experience to limit these future complications.

A concussion can be defined in several ways due to its complexity and sometimes poor understanding. This trauma has been defined by McCrory et al.[3] as an intricate pathophysiological process affecting the brain, induced by biomechanical forces. Concussion has also been defined as a traumatically induced transient disturbance of brain function and is caused by a complex pathophysiological process.[2] Despite the current research on concussions, there is no widely accepted standard definition. Variations of a general theme have been used by researchers to create their own person understanding of sport-related concussions.

The most common mechanism of injury (MOI) for this brain disturbance is by way of player-to-player contact.[42] Damage to the brain from this impact can occur on different parts of the brain. When contact is made to a stationary head, typically damage is done beneath the point of impact which is known as a coup injury.[6] Inversely, when a moving head impacts a stationary object, damage is typically done to the opposing brain also known as countrecoup.[6] Countrecoup injuries occur from the brain shifting and making contact with the cranium.[6] Harmon et al.[2] simplified the common concussion MOI as being any linear and/or rotational force that is transmitted to the brain, which causes injury.[2]

The neurometabolic cascade that takes place following traumatic brain injury is a complex process that has yet to be fully understood. Researchers have been able to make most of their conclusions from the study of different animals such as rats.[43] It can be seen in these rodent studies that immediately following a concussive blow the brain goes through a number of different changes.[43] Acute abnormalities include ionic fluxes, indiscriminate glutamate release, hyperglycolysis, lactate accumulation, and axonal injury.[44] Later steps in the physiological cascade involve increased intracellular calcium, mitochondrial dysfunction, impaired oxidative metabolism, decreased glycolysis, diminished cerebral blood flow, axonal disconnection, neurotransmitter disturbance and potentially cell death.[44] Due to post-concussive deficits resolving over time, it can be suggested that these deficiencies are likely caused from temporary neuronal dysfunction rather than permanent cell death.[44] It is worth noting that the current study does not assess injured individuals, thus the array of physiological cascades that occur following a concussion will not be discussed in further detain in this review.

Due to all of the previously stated physiological impairments, a number of symptoms may be present in individuals with mild traumatic brain injury and last anywhere from days to weeks.[1,45,46] Some of these reported symptoms include; headache, irritability, balance and memory dysfunction, impaired eye movement, confusion, amnesia, nausea, slurred speech, fatigue, sensitivity to light and sound, and sleep disturbances.[1,45,46] Previous research has shown that headache and dizziness are the most commonly reported symptoms respectively.[42,47-49]

Although these symptoms are commonly indicative of a mild traumatic brain injury, they should not be used as a standalone measure to determine the presence of a concussion. Some symptoms can overlap with other mental disorders such as sleep disturbances, depression and attention deficit disorder.[2] It is a widely accepted misconception that one must also have loss of consciousness in order to be diagnosed with a concussion. Previous studies have shown that only 10% of concussed individuals will have loss of consciousness.[3,47,49] Previously, loss of consciousness had been used to grade concussion severity. However, it is recommended by the National Athletic Trainers Association (NATA) position statement that concussions should now be evaluated, graded and treated on an individual basis.[5,7]

A study by Covassin et al.[50] demonstrated that females reported significantly more symptoms than their male counterparts following the diagnosis of a sport-related concussion. Along with having an increased number of symptoms, females were also 1.7 times more likely to be cognitively impaired[51] such as having decreased reaction time[51] and worse visual memory performance[50]. These sex differences in cognitive function following a concussion may be explained by hormonal differences, weak musculature, neuroanatomical differences or cerebral organization.[52-55] Due to having an increased number of symptoms and poorer performance on neurocognitive tests, females often take longer to recover from a concussion than males.[37,42,56]

Not only was gender shown to have multiple differences in the outcome of sport-related concussion, but the younger the injured participant, the longer it took them to return to activity.[57] High school athletes have been found to demonstrate significant memory impairments up to 7-14 days following a concussion,[58] whereas Echemendia et al.[59] found that collegiate athletes on average demonstrated no neurological impairments later than 7 days post-concussion. Specifically, some high school athletes have been found to have reaction time impairments up to 21 days following concussion.[60]

Concussion Management

Position Statements

Consensus statements for sport related concussions started to be developed in 2001.[61] This development took place in Vienna, Austria where a group of experts came together with the aim to improve the safety and health of athletes who suffer concussive injuries.[61] This conference set many of the definitions and general recommendations that we currently use today. They began by defining what a concussion is and what to expect during a clinical evaluation.[61] They expanded upon some of the things that can be expected when evaluating an athlete for a concussion. These expansions go on to include specific cognitive signs, symptoms and physical presentations.[61] Following the expected signs and symptoms, they go on to outline the recommended evaluation procedure which includes; symptom inquiry, neuropsychological assessment, and the possibility of neuroimaging.[61] Following their evaluation process they go on to discuss concussion management and rehabilitation. In this section they discuss the stepwise process that should be followed when returning an athlete to play.[61] At the conclusion of the consensus statement they wrap up by discussing the general directions they would like to go in the upcoming years. This will provide the guidelines for future drafts of the consensus statement.

The second concussion consensus meeting was conducted in Prague, Czech Republic in 2004.[62] This second gathering was to update and improve upon the previously created first statement. This second meeting maintained the same previous outline however significantly expanded on every one of its sections.[62] The first major update since the previous statement was the addition of simple and complex concussion classifications.[62] This outlined how a simple concussion resolves in a matter of 7-10 days whereas a complex concussion lasts significantly longer with more complications.[62] The next major update came with the addition of a pre-participation physical examination (PPE) section.[62] In this section they go on to explain the importance of a PPE not only to inquire information on previous concussions but to learn who is more susceptible to these future injuries.[62] Finally, the major change in the second consensus statement is the discussion of the sport concussion assessment tool (SCAT) and how it adds to the evaluation process.[62] This section explains in depth what the SCAT and its combination of several trusted assessments into one.[62]

In 2008 this group of experts came together once again in Zurich, Switzerland to address their desired updates for the concussion consensus statement. Once again this draft maintained its meticulous format with the addition of several key sections.[3] Guidelines for key evaluation scenarios were added such as; emergency room visits and same day return to play.[3] Along with the variations of specific populations such as children and elite athletes.[3] The original SCAT form received an update and is now the SCAT2 making the evaluation process more organized than ever before.[3] Finally the last major change was the discussion of sport equipment such as helmets and their benefit to concussion safety.[3]

Today we currently are under the fourth update of the concussion consensus statement which was drafted in 2012 once again in Zurich, Switzerland.[5] This update focused more on discussing current concussion concerns and addressing common questions brought up by clinicians.[5] The only major additions to the current consensus statement came in the form of the SCAT3 and the explanation of gender differences in concussion evaluation.[5]

Broglio et al.[7] have provided medical professionals with his up to date, heavily researched National Athletic Trainers Association position statement on concussions which clearly lays out concussion evaluation, management, return to play and patient education. A research based approach was used to expand on the previously determined standard of care that should be given to athletes with sport-related concussions.[7] Any athlete suspected of having sustained a concussion should be removed from play and assessed immediately by a licensed healthcare provider trained in the evaluation and management of concussions.[2] This mild traumatic brain injury should be assessed using a multifaceted approach that includes symptom inventory, balance assessment, and computerized neurocognitive testing.[3] Of these different aspects of the evaluation process, the neurocognitive assessment provides the greatest amount of objective clinical information.[8]

Neurocognitive Assessment

Neurocognitive assessment tools are used to assess participants in a number of different mental performance tasks to determine the presence of mild traumatic brain injury. The most widely used neurocognitive assessment in North America is the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) tool, which has been shown to be a valid means for evaluating a sport-related concussion.[63] This test takes about 25 minutes to complete[57] and consists of 3 main sections; 1. A demographics section, 2. A post-concussion symptom scale (PCSS) section, and 3. Neurocognitive test modules.[14]

The demographics section includes descriptive information such as years of experience playing sports, history of drug and alcohol use, learning disabilities, major neurocognitive disorders and concussion history.[14] The PCSS section asks participants to self-report a total of 22 concussion related symptoms based on how they are feeling at the current moment. This section uses a 7-point Likert scale, with zero being not experiencing and six meaning they are severely experiencing the symptom.[14] The neurocognitive test module section consists of six testing modules that are combined mathematically to produce four composite scores for verbal memory, visual memory, visual motor performance and reaction time.[64] There are five different versions of the testing modules, to minimize and control for any practice effect over multiple attempts.[57]

Multiple researchers have examined the ImPACT battery with hopes to validate its effects of properly evaluating an individual for the presence of a concussion. A study by Cole et al.[9] reported moderate to high reliability (interclass coefficients (ICC) ranging from 0.50 to 0.83) when tested again after a 30 day period. Another study by Elbin et al.[10] agreed with the previous study and reported moderate to high ICCs ranging from 0.62 to 0.85 when tested again after one year. This reliability means an individual can be tested on one day and have similar results if they are tested again in 30 or even 365 days. To go along with its moderate to high reliability, ImPACT has been shown to have high sensitivity[11-13] and specificity[11,13] when assessing for the presence of a concussion. Despite all of the research to show high sensitivity and specificity, McCrea et al.[65] suggest that no one test should be used alone for concussion evaluation. They believe that multiple evaluation tools should be used collaboratively will have higher sensitivity when determining the presence of a concussion.[65] Iverson et al.[66] have determined reliable-change index scores which allow clinicians to see if various ImPACT composite results yield a significant difference when compared to a previously taken baseline.

Gender needs to be taken into consideration when evaluating a concussion, as differences are present in neurocognitive performance when tested using ImPACT. Covassin et al.[57] reported that females demonstrate significantly worse visual memory performance, which is in agreement with Broshek et al.[51] who also reported a worsening of reaction time. Females were overall 1.7 times more likely to be cognitively impaired following a concussion than their male counterparts.[51]

Currently, clinicians can choose between a computerized desktop version and an online version when administering ImPACT. Through previous research, it has been shown that the online version has significantly less invalid baselines (4.1%) than the desktop version (10.2%) making it the smarter choice for the assessment of concussions.[67] Never the less, whatever choice the clinician makes should be consistent when testing an individual over a period of time.

The use of computerized neurocognitive assessments employing pre-participation baseline tests, followed by a series of post-concussion test have become a widely adopted element within the multidisciplinary approach to concussion evaluation and management.[5,6] In simplified terms, a baseline exam should be done prior to the start of a season in order to have a reference for post-concussive neurocognitive tests. If a concussion is suspected, neurocognitive testing should be implemented immediately due to the possibility of under-reporting by the athlete. Van Kempen et al.[15] pose a serious concern that athletes will under-report concussion related symptoms in an effort to expedite their return to play, thus making neurocognitive testing important when a concussion is suspected. A study by Broglio et al.[64] goes a step farther to say that 38% of post-concussive individuals still have impaired neurocognitive performances when asymptomatic. The previous two studies have provided evidence to show why it is important to test individuals using a neurocognitive test such as ImPACT when determining return to play decisions following mild traumatic brain injury.

It is recommended that more than one assessment tool be utilized in the evaluation of a concussion. The King-Devick Test was created to add to the concussion evaluation battery and provide clinicians with a simple and efficient sideline evaluation tool. The test involves reading aloud a series of random single digit numbers from left to right on a demonstration card and three testing cards.[18] The participant will be evaluated based on their total time to perform this rapid number naming on all three test cards and should ideally take less than two minutes total to perform.[18] The results are compared to a pre-concussive baseline the athlete performed prior to athletic participation. During the baseline assessment, every individual is tested twice with the fastest time recorded.[19] Once an individual is suspected of a concussion, they will complete the test battery under the same conditions as their baseline. A worsening of overall time will indicate the possible presence of a concussion and further evaluation is required.[68]

There are two forms of the test the clinician may utilize, one being spiral bound testing cards, and the other via a mobile application on an iPad or tablet.[18] Leong et al.[18] have determined that King-Devick results are not effected by environmental noise, thus making the test relevant in any environment. A 4.4 second decrease was identified in concussed individuals when compared to their baseline.[18] However, a learning effect was noted in healthy participants, with an improvements being made after just two tests. [18-22,68,69] Previous investigations have shown a 2.2-3.1 second improvement in consecutive tests, supporting this learning effect.[19,20,22,68,69]

The King-Devick test requires eye movement, language function and attention in order to perform tasks, which have been shown to reflect suboptimal brain processing in the presence of a concussion.[18,20-22,69] Previous research has reported that the King-Devick test has high reliability when tested over time.[19,68] Due to a lack of research on this new assessment tool, Vartianinen et al.[70] have come up with normative data to assist clinicians when interpreting King-Devick results. They have determined that times less than 33.8 seconds are considered ideal, 33.9-56.6 are acceptable, and times greater than 56.7 seconds are considered extremely slow and further evaluation is warranted.[17]

Despite ImPACT and the King-Devick test being highly valid and reliable, a concussion should be evaluated with multiple assessment tools to increase sensitivity to the injury. The Sport Concussion Assessment Tool 3 (SCAT3) provides clinicians with several evaluation tools in one assessment. The SCAT3 evaluates individuals in a number of aspects such as; concussion symptoms, cognition, balance, Glasgow Coma Scale and some neurological signs.[71] Once completed, a combined total score out of 100 is produced with a lower score representing poor performance. Within the SCAT3 are multiple tools that can act alone and add to the concussion assessment process such as the Balance Error Scoring System (BESS).

The BESS test is a popular balance assessment tool which is often used on the sideline of events. This test provides clinicians with an overall error score in 6 different balance trials.[72] This error score is compared to the individual's pre-concussion baseline to determine the presence of any deficits. However, as stated earlier, a single test should not be used as a stand-alone assessment of a concussion. The BESS test should be used in addition to a neurocognitive assessment tool.

Return to Activity

Individuals who have been diagnosed with a concussion should be withheld from any mental or physical activity that increases symptoms or when symptoms are still present.[2] It is not uncommon for females to take longer to recover from these post-concussive symptoms than males, so patience is advised when treating female athletes.[51,73-76] With that being said, studies suggest that 80-90% of athletes will have a resolution of symptoms within 7 days of the diagnosed concussion.[42,47,48] Gradual physical activity may begin when the athlete is free from post-concussive symptoms and has a normal neurocognitive exam when compared with their baseline. The increase in return to play activity should be conducted in a stepwise fashion in physical demands, sport-specific activities and physical contact.[2] Once this gradual increase in activity has begun, all progress should cease if the individual develops any symptoms and must wait until symptoms subside before starting the process over.[2] All post-concussive athletes must be symptom free at rest, as well as during each level of activity in order to be returned to full participation.[2]

It is critical that athletes show no cognitive impairments prior to retuning to full sport participation. Studies suggest that a second injury before the brain has recovered, results in worsening cellular metabolic changes and more significant cognitive deficits.[43,55,77-79] This second injury is often termed second impact syndrome (SIS) and mainly occurs in athletes under the age of 18.[2] It is believed that youth are more susceptible to SIS than adults since they do not have a fully developed brain.[2] SIS potentially causes a vascular engorgement in the brain that leads to an increase in intracranial pressure, brain herniation, coma or even death.[2] Due to the lack of agreement on SIS, the occurrence of this injury has gone underreported making it difficult to know the exact prevalence of the injury.[2] The ultimate goal of the clinician's return to play protocol should be to avoid SIS and any further injury that comes from the initial concussion.

With the goal of the athlete's safety in mind, it is of high importance to ensure everything is being completed to properly evaluate and manage sport-related concussions. It is important to know what tools are available for the evaluation process and how to properly utilize them. Although honesty is emphasized with subjective symptom scores, athletes may be deceptive when reporting their cognitive state.[80,81] Some individuals may even go as far as to alter their state of mind to decrease symptoms or improve neurocognitive performance. These alterations could range anywhere from pain relievers to stimulants for the purpose of neurocognitive improvement.[2]

Reaction Time

Reaction time seems to be a term used in every sport setting. Some people may use it to explain a baseball player reacting to a pitch, others may use it to discuss how a hockey goalie is able to block a shot. However it may be used in an athletic setting, the true definition as defined by Shelton et al.[82] is the elapsed time between the presentation of a sensory stimulus and the subsequent behavioral response. This response to a stimulus is important to every athlete. Having good reaction time allows someone to act slightly faster than their opponent, thus giving them an advantage in competition.

As with concussions, reaction time has also become an increasingly popular subject of study due to its athletic importance. It has been shown that head injuries such as concussion, have a detrimental effect on reaction time.[66,83-85] Eckner et al.[84] demonstrated an 8.4% decrease in reaction time following a mild traumatic brain injury when tested using a drop item technique. Iverson et al.[66] provided similar results when they concluded that 70% of their subjects had decreased reaction time scores following a concussion. This decrease in reaction time following mild traumatic brain injury provides clinicians with another aspect in their evaluation process. Any athlete suspected of having a concussion should have reaction time evaluated to determine if any deficits are present. In contrast, a slight improvement in reaction time has been seen following the ingestion of caffeine.[29,34,86,87] This finding may allow athletes who supplement with caffeine to mask the deficits in reaction time following a concussion.

Caffeine

Caffeine is the most widely consumed psychoactive drug in the United States.[88] One study reported that 85% of people consume at least one caffeinated beverage per day.[89] This leads to adults ingesting an average of 164 mg of caffeine per day.[89] Typical sources of caffeine entail: chocolate, coffee, tea, energy shots, energy drinks, pre-workout supplements, and carbonated soft drinks such as cola. Despite chocolate being an ever so popular dessert, only 2 percent of total caffeine consumption comes from food sources in an adult population.[89] The rest comes from beverages.[90]

Coffee is the most common ingested beverage by American adults. Coffee makes up 104mg of the average 164mg ingested daily.[89] A single 8oz cup of coffee can range from 48mg- 502mg of caffeine.[89] This wide range is ultimately effected by the origin of the coffee bean crop, and the time and temperature the beverage is prepared.[89]

Carbonated soft drinks are also in high demand due to its perceived mental effects and enjoyable flavor. Since carbonated soft drinks have a sweet flavor, they are most popular in the youth population compared to adults.[90,91] However, soft drink consumption has been on the decline in recent years[89], possibly due to the use of added sweeteners.

Other forms of caffeine such as energy shots, energy drinks and pre-workout supplements differ in volume, ingredients, levels of caffeine, sugar, vitamins and other stimulants.[92] These supplements are not regulated by the U.S. Food and Drug Administration (FDA) so the amount of ingredients may vary by serving. The caffeine content can range anywhere from 60-200mg of caffeine making the perceived effect strength unknown.[31,93,94] The ingestion of these products should be monitored carefully and should not exceed the recommended daily amount.

Following consumption, caffeine is metabolized by the liver and is made readily available in the blood. It has been reported in several studies that caffeine reaches peak plasma concentration 45 minutes following liquid caffeine ingestion.[95-97] Caffeine will produce a mild neurostimulant effect by antagonizing adenosine, thus disinhibiting neuronal firing throughout the brain.[25,26] This counter effect on adenosine receptors will improve attention, reaction time, memory and verbal reasoning.[98-102] It has also been shown to improve wakefulness and mood along with decreasing mental fatigue.[31,92,98,103,104]

Not only does caffeine effect mental abilities but it has also been shown to have improvements on physical performance. The variety of known mental improvements can also delay perceived fatigue during activity. As stated earlier, caffeine will cause a blockade of adenosine receptors, which will prevent a decrease in neuronal activity and subsequently increase muscular recruitment.[105] Previous research has shown improvements in sprinting,[28] as well as improvements in the identification of targets during a shooting contest.[106]

Despite all of the benefits from caffeine, it is recommended not to exceed 400 mg per day to avoid negative health effects.[107,108] Also, exceeding 400 mgs puts an athlete's participation status in jeopardy, caffeine is well regulated by governing athletic bodies and does not allow more than 15 micrograms/ml of urine when tested.[109] This regulation is to promote fair competition and is in place to maintain athlete's safety.[109] Excessive caffeine intake has been associated with an increase in anxiety, headaches, nausea and nightly restlessness.[107,108] Although these side effects are temporary and less severe in nature, frequent abusers could develop high blood pressure, which will negatively affect the cardiovascular system over time.[110-112] Withdrawal symptoms can occur in individuals who abstain from normal caffeine consumption and can peak in intensity between 20-51 hours.[113] Of the typical withdrawal symptoms, headache and increased fatigue are most prevalent.[113] Individuals who abide by the daily recommended allowance of caffeine can reap benefits such as lowering risk of type 2 diabetes, Parkinson's disease, and several types of cancer.[114-117]

It is clear that caffeine has mental and physical benefits if utilized properly. Energy shots provide athletes with a high amount of caffeine in an efficient 2-4 ounce liquid shot. Currently there are multiple brands of energy shots on the market, with 5 Hour Energy® being extremely popular.

5 Hour Energy® is the most marketed and recognizable energy shot available. It can be found in a number of different supermarkets, gas stations and fitness stores. This energy shot combines 30mg of Niacin, 40mg of vitamin B6, 400mcg of folic acid, 500mcg of B12, 18mg of sodium and 1870 of an energy blend into a small 1.93 fl. oz container.[118] According to the product's website, the energy blend is broken down into taurine, Glucuronic Acid, Malic Acid, N-Acetyl L-Tyrosine, L-Phenylalanine, Citicoline and 200mg of caffeine.[118] With its small size, pre-made form and variety of flavors, this energy shot provides individuals with an efficient and well liked caffeinated option.

A study by Powers[34] assessed the influence of a pre-workout powdered supplement (Jacked 3D) on reaction time, memory and motor processing speed during the ImPACT battery. Participants in his study were broken up into three groups; a stimulant group, a placebo group and a control group. Every participant received the intervention 30 minutes prior to taking the test. Despite comparing several outcome variables, only significant improvements in reaction time and impulse control following caffeine ingestion were observed.[34] However, with a powdered supplement, it is hard to determine the exact amount of caffeine every scoop contains. Also, Powers[34] states he could not be sure the improvements were from the caffeine or from the dimethylamylamine (DMAA), which is another stimulant present in the pre-workout supplement

CHAPTER III

RESEARCH DESIGN

Materials and Methods

Design

The current study was a randomized, single-blinded crossover study. The independent variables were the substance ingested, (5-hour energy and placebo) and the testing sessions (session 1 and session 2). The dependent variables included, ImPACT reaction time composite scores and the overall King-Devick time.

Participants

Eighteen (14 male and 4 female) healthy collegiate students (Age = 21.7 ± 1.4 years, Height = 175.0 ± 9.1 cm, Weight = 75.6 ± 12.5 kg) participated in this study. Participants were excluded from the study if they had a history of high blood pressure, diagnosed heart condition, neurocognitive disorder or clinically diagnosed mental illness, more than one concussion in their lifetime or one within the last year, caffeine sensitivity, currently taking any prescribed medications, except birth control, ingest more than 500mg of caffeine daily (which may be equivalent to more than two cups of coffee per day), or have been exposed to ImPACT or Kind-Devick tests within the last year. Participants signed an informed consent form before taking part in the study. The institutional review board approved this study. All participants were instructed to not have any caffeine the day of testing.

ImPACT

ImPACT is a widely used tool to assess the athletic population for the presence of a concussion[12] and has high reliability up to 50 days after sustaining a concussion.[14] The ImPACT takes approximately 25 minutes to complete and has 5 different test versions to minimize and control for practice effects.[57] ImPACT is broken down into 3 sections: demographics of the participant (ex. Age, gender, height, weight, etc.), current health symptoms (22 concussion related symptoms on a 0-6 scale) and neurocognitive testing modules. The modules test the participants in the previously stated 5 aspects associated with a concussion: concentration, attention, memory, visual motor speed and reaction time.[64] For the current study, the online version of ImPACT (ImPACT Applications Inc, Pittsburgh, Pennsylvania, USA) was utilized to test every participant and was completed under the supervision of a Certified Athletic Trainer.

King-Devick

The King-Devick test was developed to give clinicians an efficient and reliable sideline concussion assessment tool. The King-Devick test requires eye movement, language function and attention, which have all been shown to reflect suboptimal brain processing in the presence of a concussion.[19-22,69] This test typically takes less than two minutes to administer and can be done electronically or via spiral bound testing cards.[18] For the current study, a copy of the electric version was printed off and administered for testing. Participants were asked to read aloud a series of single digit numbers from left to right as fast as possible without making a mistake. The total time to complete three testing cards was assessed and compared across conditions. Typically, every participant is allowed one practice card to familiarize themselves with the process before testing. The King-Devick test has been shown to have high reliability[19,68] when tested over time, thus making it a valuable option in the concussion evaluation process.

Caffeine

There were multiple products to choose from when determining the proper amount of caffeine for our participants. 5-hour Energy® is a convenient and easily accessible form of caffeine, due to its high potency and small size. This energy shot combines 30mg of Niacin, 40mg of vitamin B6, 400mcg of folic acid, 500mcg of Vitamin B12, 18mg of sodium and 1870mg of an energy blend into a 1.93 fl. oz. container as shown on its supplement facts panel.[35] According to the product, the energy blend is broken down into unknown quantities of Taurine, Glucuronic acid, Malic acid, N-Acetyl L-Tyrosine, L-Phenylalanine, and Citicoline.[35] The caffeine content in 5-hour energy is 200mg per shot, which is equal to a strong cup of coffee.[35] It has been reported that caffeine reaches peak plasma concentration 45 minutes following oral ingestion.[95-97] With this in mind, our participants were tested 45 minutes following ingestion of the energy shot.

Procedure

Testing

The current design was a single-blinded randomized cross-over study where the participant acted as their own control. The individuals being tested were blinded to the substance they ingested for each day of testing. They were instructed not to ingest any caffeinated drinks the day of testing, to avoid over consumption. Once the participant arrived, they were instructed to pick a number from a concealed envelope. An even number represented the caffeine intervention for the initial test while an odd number represented the placebo (fruit juice and water) intervention. The drinks were prepared in plastic cups to prevent the participant from knowing if it was the energy shot or placebo. Following ingestion of the beverage, participants were instructed to sit for 45 minutes. This 45 minute break allowed every participant to get close to their peak plasma concentration as reported by previous research.[95-97] During the 45 minutes, participants were able to watch television, listen to music or visit social media. These restrictions were enforced for every participant to ensure minimal mental stimulation prior to testing. To limit the effect of caffeine on one particular concussion assessment, the order of testing (ImPACT vs King Devick) was randomized and placed in a concealed envelope for each participant. The participant's assessment order remained consistent during the study. Every participant was allowed one practice card for the King-Devick test, then they were assessed using the three testing cards. The total time to complete all three cards was recorded with participants expected to take no longer than two minutes. ImPACT was initiated under the supervision of a certified athletic trainer who was available throughout the test to answer any questions. The participants were instructed to complete every aspect of the test with maximal effort. Following completion of the test, participants were asked to return exactly one week later to receive the opposite intervention. Participants were tested at the same time of day, on the same computer, in the same setting and under the supervision of the same certified athletic trainer in order to maintain consistency.

Data Analysis

After completion, participants' total King-Devick times and the reaction time composite score for ImPACT were recorded. Four paired samples t-tests were used to evaluate the difference between the caffeine induced scores and the placebo scores for both the King-Devick and ImPACT tests, as well as the time to complete each test during session 1 and testing session 2. All data was analyzed using SPSS 21 with alpha set *a priori* at $\alpha \leq .05$.

CHAPTER IV

ANALYSIS OF THE DATA

Results

A statistically significant difference was noted in the RT composite score following ingestion of the stimulant compared to the placebo substance (P=.007; Table 1). A moderate effect size for the difference in ImPACT RT composite score was observed 0.60 (-.07-1.27). Despite this improvement on ImPACT, the KD overall time recorded no change between interventions (P=.118; Table 1). Other measures from ImPACT were not measured for the current study.

The KD test resulted in a significant improvement between session 1 and session 2, suggesting a practice effect (P≤.001; Table 2). This between session improvement recorded a low to moderate effects size of 0.54 (-.13-1.21). A practice effect was not noticed between session 1 and session 2 of ImPACT (P=.341; Table 2).

TABLE 1
Testing Performance Under Each Intervention

	Caffeine		Placebo		
	Mean	SD	Mean	SD	P-Value
ImPACT RT	0.53 sec	0.05 sec	0.56 sec	0.07 sec	0.007
King-Devick	36.2 sec	5.4 sec	37.6 sec	5.5 sec	0.118

TABLE 2
Testing Performance Between Sessions

	Session 1		Session 2		
	Mean	SD	Mean	SD	P-Value
ImPACT RT	0.55 sec	0.07 sec	0.54 sec	0.06 sec	0.341
King-Devick	38.2 sec	5.6 sec	35.5 sec	5.0 sec	<0.001

CHAPTER V

SUMMARY, CONCLUSION AND RECOMMENDATIONS

Discussion

The focus of this study was to evaluate a caffeinated energy shot's effect on the ImPACT RT composite score along with the KD overall score. There was an improvement of 0.03 seconds in the ImPACT RT composite score following ingestion of caffeine when compared to ingestion of a placebo. This improvement means participants on average were able to identify a computerized stimuli 0.03 seconds faster, 45 minutes after ingesting caffeine than fruit juice. Despite having an improvement on ImPACT, there were no differences noticed for the KD test. Another result worth noting was the improvement between testing session one and testing session two for the KD test regardless of solution ingested. This decrease in overall time suggests the presence of a practice effect. The practice effect was relatively high, with participants improving their overall time by almost 3 seconds. A practice effect was not noticed for the ImPACT battery.

Due to their varying effects on each individual, concussion diagnosis can pose a challenge throughout the evaluation process. This head trauma has been shown to have detrimental effects on reaction time[66,83-85] and decision making.[119] The use of a computerized neurocognitive evaluation program provides clinicians with the greatest amount of objective clinical information on these deficits, resulting in a confident diagnosis.[8] Due to this reliance on the neurocognitive aspect of evaluation, it is critical to verify the tools created to assess athlete's cognitive function. ImPACT and the KD test have been shown to be valid[18,63] and reliable[9,10,19,68] when assessing mental deficits in concussed individuals. Both ImPACT and the KD test are taken prior to the start of athletic participation to act as a baseline for future post-injury testing.[5,6] Eliminating any potential threat to the post-concussive testing process may ensure maximum safety when returning an athlete to full contact participation. The present study suggests that a caffeinated stimulant ingested prior to neurocognitive testing may help expedite this step in the return to play process.

This current improvement in RT is in agreeance with several studies that present an increase in cognitive performance following the ingestion of caffeine.[29,86,120] These studies include specific increases in stimuli recognition[86,120] and response to a physical presence.[29,106] In concurrence with cognitive improvement, there have been several studies reporting caffeine's increased effects on physical performance, such as sprint training[28,121,122] and power output.[86,123,124] Similarly to the current study, Powers[34] looked at caffeine's effect on every composite score produced by ImPACT. He reported improvements in RT and cognitive-efficiency index scores following stimulant ingestion compared to participant's controlled state. To date there are no studies that have evaluated caffeine's effect on KD scores.

The participants of the current study were randomly assigned to which intervention they received the first day of testing. This randomization along with testing one week apart were in efforts to combat any possibly learning effect for either assessment. Despite all preventative measures, there was a practice effect noticed for the KD test. This is not the first study to see this effect for the KD test, as several studies have noticed a practice effect on healthy individuals when tested repeatedly over time.[18,20,125,126] ImPACT however, did not have a practice effect which could be accredited to its several different versions of the test module.[34,57]

Participants for the current study performed the KD test with an average time of 36.2 seconds with caffeine and 37.6 seconds with the placebo. This suggests there is no difference between the two interventions, thus suggesting that caffeine is not a threat to the KD test. On average, participants performed the KD test in 38.2 seconds on their first visit and 35.5 seconds on their second visit, clearly demonstrating a learning effect. With this learning effect in mind, it is recommended that the KD test not be a stand-alone measure to determine the presence of mild traumatic brain injury.

5-hour energy® was selected for the current study because of its easy accessibility for a wide array of people. 5-hour energy® could provide a concussed athlete with an effective and convenient form of caffeine prior to taking any neurocognitive assessments. This 1.93 fl. oz. container contains 200mg of caffeine which will provide as much energy as a strong cup of coffee.[118] It has been reported that caffeine will reach peak plasma concentration between 15 and 120 minutes[25] with more specific research suggesting caffeine reaches 99% absorption around 45 minutes following ingestion.[95-97] With these recommendations in mind, the current study enforced a 45 minute wait period between the intervention and the first neurocognitive assessment. This wait period ensured full absorption of the caffeine prior to testing.

The reliable-change (RCI) methodology allows clinicians to estimate measurement errors which surround test-retest scores.[66] A clinician can be more confident in an ImPACT composite score if it exceeds this RCI score, ensuing actual mental deficits are present. RT scores for the current study were improved by 0.03 seconds following the stimulant ingestion, which does not reach the recommended reliable-change index score of 0.06 seconds for RT.[66] Despite not reaching this index score, the current study suggests that caffeine may act as a threat to the RT composite score of the ImPACT protocol. This threat could allow an athlete to be returned to participation prior to full recovery, resulting in further injury. Inversely this threat could also affect baseline scores, potentially delaying the return to play protocol for healthy individuals. One such injury is Second Impact Syndrome (SIS). SIS can cause vascular engorgement in the brain that leads to an increase in intracranial pressure, brain herniation, coma or even death.[2] Following a concussion, it should be the clinician's main focus to return an athlete to participation safely to minimize the risk of SIS.

The present study has a number of limitations, with its small sample size of eight-teen and healthy, non-concussed, population being the most important. These mentioned limitations make it challenging to generalize the results to concussed individuals. Another limitation to the current study was whether it is the caffeine's effect that caused changes in RT or if the B vitamins found in 5-hour energy® had an effect. Future research should evaluate several other common forms of caffeine such as coffee, energy drinks, or caffeinated soft drinks. Some other limitations were related to participant regulation, there are no certainties that individuals maintained their normal daily activities such as food intake or caffeine consumption. Participants were also assumed to have put forth maximum effort during all testing for the present study. Future studies should have stricter participant regulations to limit any outside influence on the testing results. Finally, due to the inability to directly measure blood concentration, it is uncertain if full caffeine metabolism occurred for every individual. Based on the current study and the study done by Powers[34] it is recommended that clinicians inquire about caffeine consumption prior to any neurocognitive evaluation. This inquisition should either be the responsibility of the clinician or a questions added to the ImPACT demographic section.

Conclusion

The current study looked at caffeine's effect on ImPACT's RT composite score and overall KD time. Caffeine improved RT scores on ImPACT, with no overall change in KD times. These results suggest that caffeine may pose a threat to RT composite scores during the ImPACT battery. Based on the results of this study, it is suggested that clinicians inquire about recently ingested stimulants prior to neurological testing. This verification will ensure minimal threats to the ImPACT protocol, resulting in safe return to activity.

This study also evaluated each evaluation tool for a practice effect. As mentioned earlier, the current study found a statistically significant improvement from session one to session two of the KD test. This improvement warrents caution when testing individuals several times throughout the evaluation or return to play process. Based on the current results and the results of several others[18,20,125,126], it should be recommended that the KD test not be used as a stand-alone assessment during the concussion evaluation process but rather in conjunction with several other evaluating techniques

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