ADHD Medication and Exercise  
The Combination’s Implications on Sport Safety

Tag Words: ADHD; exercise; adderall; sport; cardiovascular risk; correlation

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Summary

Various medications are used to treat attention-deficit/hyperactivity disorder (ADHD) Side effects, specifically on the cardiovascular system are examined. A growing number of tragic physiological occurrences have been observed when underlying heart conditions are exacerbated with the stresses of exercise and sports. We sought to determine whether there was a link between the cardiovascular events and possible overlaps with the use of ADHD medication.

Video Link: http://youtu.be/tc-51h1OKW8

Potential Physiological Dangers Associated with ADHD Medication and Exercise

ADHD Overview (RL)

Among children, attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed neurobehavioral disorder (Wigal, 1). It is characterized by the three main symptoms of hyperactivity, inattention, and impulsivity (Lakhan, 661). An individual with a principally inattentive form of ADHD has difficulty finishing tasks or staying focused. They may also struggle to organize and complete tasks. Individuals with ADHD who suffer from hyperactivity and impulsivity have trouble maintaining stillness and constantly interrupt. Additionally, a person may experience a mixture of the two previously mentioned types (Center for Disease Control and Prevention, 2013).

Originally thought to affect only children, it is now known that greater than 50% of individuals with ADHD during childhood continue to experience symptoms into adolescence and adulthood (Baron, 610). Overall, approximately 4% of adults have been diagnosed with ADHD (Lakhan, 661). The disorder was initially limited to children because adults do not normally express the same actions as children. For example, adults suffering from ADHD do not typically run around a house or public setting. Attention-deficit/hyperactivity disorder diagnosis is a difficult proposition as many psychiatric disorders have similar symptoms (Center for Disease Control and Prevention, 2013). In many cases the American Psychiatric Association's Diagnostic and
Statistical Manual of Mental Disorders – IV (DSM-IV) is used by mental health professionals to properly identify the disorder (American Psychiatric Association, 2013). Diagnosis of ADHD is based upon a the demonstration of a certain number of standard symptoms.

Currently, no single etiology exists for attention-deficit/hyperactivity disorder. It is expected that both genetic and environmental aspects are contributing factors (Salmeron, 489). Attentional regulation in the prefrontal cortex of the brain seems to be negatively affected in individuals suffering from ADHD. Research has indicated that dysregulation in catecholamine (i.e. dopamine and norepinephrine) circuits within the prefrontal cortex has shown to play a major factor in the onset of ADHD (Wigal, 1). Each catecholamine has an important function in working memory, which is associated with both the prefrontal cortex and aspects of attention. To state differently, low levels of catecholamines may contribute to inattentiveness, while high levels are associated with hyperactivity (Wigal, 2).

Most forms of ADHD treatment take advantage of the previously depicted catecholamine dysfunction. While behavioral therapy is widely used to treat ADHD, pharmacological drugs, particularly stimulants, positively affect 70-80% of children (Center for Disease Control and Prevention, 2013). Positive improvement is similar in adolescents and adults. However, despite positive effects of such drugs, it has been suggested that they also carry inherent risks.

Overview of ADHD Medications and their Side Effects (MM, CM)

ADHD medications can be grouped into two categories, methylphenidates and amphetamines. Both methylphenidates and amphetamines include immediate, short-acting, and long-acting subtypes. All subtypes and respective characteristics are shown in Table 1 (Appendix 1). The FDA issued a warning about the risk of drug abuse with amphetamine stimulants and are also concerned with the possibility that both types of medication may increase the risk of heart problems. In 2006, advisory committees for the FDA acknowledged the potential cardiovascular risks associated with ADHD stimulants by recommending label changes to such prescriptions. The label changes would include a black-box warning, indicative of serious addictive and possibly life-threatening side effects (Cooper et al., 1901). Additionally, current labels warn that the medications should not be taken by individuals with structural heart conditions or pre-existing cardiac disturbances. Medication guides are also provided to patients every time an ADHD stimulant is filled. These guides warn that sudden death has occurred in individuals with such pre-existing conditions or in those with a family history and/or risk factors for cardiovascular disease (FDA, 2007).

As with any medication being taken, there are always side effects. ADHD medications are controlled prescriptions supposedly monitored by physicians and pharmacists, but casualties may arise when the drugs are improperly used or when given to the wrong individual.
Table 2 (Appendix 2) depicts a list of certain ADHD medications and their side effects. Some of the common medications not listed include adderall which can produce cardiovascular and high blood pressure problems, nervousness, difficulty breathing and weight loss. The effects of ADHD stimulants on the catecholamine response may produce additional physiological changes like increased heart rate and increased stroke volume (Wigal, 2). ADHD is prescribed for a medical reason; the nonmedical or improper usage of these drugs can bear many side effects to the individual taking them. The paper will proceed with a further examination into sudden cardiac death associated with ADHD stimulants. Particularly, the effects of strenuous physical activity in combination with the drug-use will be explored.

The Effects of Exercise on ADHD (RL)

In many circumstances, individuals with attention-deficit/hyperactivity disorder utilize a treatment strategy that incorporates both medication and behavioral therapy. With the potential adverse side effects associated with various pharmaceutical drugs, other solutions to combat ADHD have been investigated. One such alternative to medication treatment appears to be the institution of simple exercise. Research has indicated that exercise induces a catecholamine response similar to the one in which ADHD medications alter dopaminergic and adrenergic pathways in ADHD patients (Wigal, 2012). Increases in exercise intensity produce increases in catecholamine release in a dose-response relationship (Rethorst, 2009). Particularly, these catecholamine increases can be observed in areas of the brain governing executive function and attention (Wigal, 2012). Circulating epinephrine, norepinephrine, and dopamine all increase in the prefrontal cortex and hippocampus as exercise intensity increases (Rethorst, 2009). Because those areas are associated with attentional mechanisms, it is believed that exercise utilizes a similar strategy as pharmaceutical drugs to treat ADHD.

Additionally, neurotropic factors in the brain appear to play an important role in the pathogenesis of ADHD (Ma, 2008). For example, decreased levels of brain-derived neurotropic factor (BDNF) in the hippocampus have been most closely associated with various mental disorders such as ADHD (Kim et al., 2011). Neurotropic factors help to control neuroplasticity in the brain by increasing the number of synapses between neurons, primarily in the hippocampus (Kim et al., 2011). Exercise, once again, can be used to treat this deficiency in ADHD patients. Exercise can produce an increase in neurotropic factors, especially BDNF, to increase attentional aspects like learning and memory (Ma, 2008). The potentially harmful side effects of medications can, therefore, be avoided once again.

A relatively large gap exists in the portion of exercise science literature that concerns ADHD. Most published studies and exercise interventions concern children with ADHD, and little has been researched that would be capable of generalizing the positive effects of exercise to older populations. Most of the studies to date have shown evidence of dysfunction in catecholamine response and reception as previously explained, yet none have demonstrated long-term effects of
the proposed solution of exercise. Lastly, and possibly most important, there seems to exist this
notion of substituting certain medications with exercise, but no hard evidence has shown exercise
can completely replace pharmaceutical drugs in ADHD patients. If anything, exercise, in
combination with continued behavioral and drug therapies, can help to alleviate problems
associated with the disorder. However, this presents many questions to be answered.
Specifically, can the body be overloaded with a catecholamine response when exercising in
combination with continued drug therapy? What negative outcomes could arise from stressing
the human system (i.e. exercise) while at the same time creating an increased adrenergic
response due to medication? The pair could produce potentially deadly effects on both the
cardiovascular system.

**Cardiovascular Risk and Incidence Among Athletes (CM)**

Although each aforementioned medication has different characteristics and mechanisms of action,
for the purpose of this research, duration of action may be the most important characteristic to
consider when exercising or engaging in high intensity sport activity. If there is indeed a
correlation between stimulants prescribed for ADHD and increased cardiovascular risk with
exercise, athlete users must be warned, especially if the medication is long-acting and creates an
overlap between its duration of action and playing time.

Adderall, as well as other stimulants targeted to help mitigate the effects of ADHD, helps to
lower perceived exertion, while raising heart rate (Ireland, 2011). So while an athlete may think
or feel as though they are not fully exerting themselves, their body’s physiological changes may
suggest otherwise. This can present a danger to the cardiovascular system because the body is
performing beyond what it can handle, resulting in a higher risk of injury, a cardiovascular event,
or even death (Ireland, 2011). “Sudden cardiac death, or SCD, is the leading cause of death in
young athletes” (Drezner & Corrado, 2011). Frequency and incidence of SCD is not exactly
known and may be underestimated due to varying methodology (Drezner & Corrado, 2011).
Table 3 shows the reported incidences of SCD in several youth and young adult populations,
including athlete demographics.

Misuse of prescription stimulants, such as Adderall, is common among college aged students and
athletes. Athletes taking prescription stimulants to enhance sports performance should be aware
of the potential adverse effects on cardiovascular function, especially if possibility of a heart
condition may be present, which can usually be detected through electrocardiogram (ECG)
screening.

Stimulants are classified as Schedule II drugs, meaning they provide beneficial effects but also
have high abuse potential (Lakhan & Kirchgessner, 2012). “The nonmedical use of prescription
stimulants represents the second common most form of illicit drug use in college, second only to
marijuana use” (Lakhan & Kirchgessner, 2012). Benefits of taking Adderall, and other
stimulants aimed at increasing focus, are widely recognized and referenced in the media, while potential risks and adverse effects are much less known.

Table 3: Incidence of Sudden Cardiac Death in Children and Young Adults

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Methods and Reporting System</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Camp et al</td>
<td>High school and college athletes aged 13 to 24 years (United States)</td>
<td>Public media reports and other reported cases</td>
<td>1:300 000</td>
</tr>
<tr>
<td>Maron et al</td>
<td>High school athletes in Minnesota aged 13-19 years (United States)</td>
<td>Catastrophic insurance claims</td>
<td>1:200 000</td>
</tr>
<tr>
<td>Eckert et al</td>
<td>Military recruits aged 18 to 35 years (United States)</td>
<td>Mandatory, autopsy-based</td>
<td>1:9000</td>
</tr>
<tr>
<td>Drezenner et al</td>
<td>College athletes aged 18 to 23 years (United States)</td>
<td>Retrospective survey</td>
<td>1:67 000</td>
</tr>
<tr>
<td>Corrado et al</td>
<td>Competitive athletes aged 12 to 35 years (Italy)</td>
<td>Mandatory registry for SCD</td>
<td>1:25 000</td>
</tr>
<tr>
<td>Maron et al</td>
<td>Competitive athletes aged 12 to 35 years (United States)</td>
<td>Public media reports and other electronic databases</td>
<td>1:166 000</td>
</tr>
<tr>
<td>Drezenner et al</td>
<td>High school athletes aged 14 to 17 years (United States and Canada)</td>
<td>Cross-sectional survey</td>
<td>1:23 000</td>
</tr>
<tr>
<td>Atkins et al</td>
<td>Adolescents and young adults aged 12 to 24 years (United States and Canada)</td>
<td>Prospective, population-based, EMS reports</td>
<td>1:27 000</td>
</tr>
<tr>
<td>Chugh et al</td>
<td>Children in Oregon aged 10 to 14 years (United States)</td>
<td>Prospective, population-based, EMS/hospital reports</td>
<td>1:58 000</td>
</tr>
<tr>
<td>Asif et al</td>
<td>College athletes aged 17 to 23 years (United States)</td>
<td>NCAA resolutions database, public media reports, and catastrophic insurance claims</td>
<td>1:45 000</td>
</tr>
</tbody>
</table>

EMS, emergency medical services; NCAA, National Collegiate Athletic Association; SCD, sudden cardiac death.


Linking High Intensity Activity to Cardiovascular Events, Cardiovascular Monitoring (CM)

First, it is important to explore sudden cardiac events that occurred during professional sports or during exercise in order to search for a link between stimulant use, the cardiovascular system, and sports. For example, there is a high frequency of cardiovascular injury or death in professional soccer, notably in the media including two European pro-footballers. On April 14, 2012, an Italian footballer who played midfield for Livorno suffered a cardiac arrest on the field (Baxter, 2012). Although medics attempted to revive him with a defibrillator, Piermario Morisini, 25, died in the ambulance on the way to the hospital. Morisini’s shocking death occurred just weeks after Fabrice Muamba, a midfielder for Bolton of the English Premier League, suffered a cardiac arrest. Muamba, 24, miraculously survived the heart attack after his heart stopped for 78 minutes (BBC News, 2013). He was hospitalized for a month before being released and subsequently retired from football (BBC News, 2013). Now a year later, the Football Association (FA) of England has teamed up with the British Heart Association to make defibrillators readily available in non-league football and other clubs (BBC News, 2013).

An Indian footballer’s recent cardiac arrest proved to be fatal. In March 2012, D. Venkatesh, a midfielder for the A division club Bangalore Mars, collapsed and died in a local league game (Associated Press, 2012). He was only 25 years old. What sets this incident apart from the incidents involving Morisini and Muamba is that there was no on-site medical care. Venkatesh did not receive adequate oxygen, proper medical care, and there was no ambulance present (Associated Press, 2012).
It is unclear whether these athletes mentioned above were prescribed stimulants that contributed to their non-fatal or fatal cardiovascular arrests. However, their cases help to establish a link between high intensity sport activity and increased risk for heart attack and cardiovascular death. All athletes were very young, and our research up to this point would suggest that they may have had a pre-existing condition that contributed to their injuries. If this is the case, EKG/ECG screening may provide indication of such conditions before participating in any life-threatening physical activity, such as professional sport.

Adequate screening prior to sport participation is a heavily debated topic in the world of sport safety and cardiology, and not all governing bodies have adopted the same practice. Major League Soccer of the United States has a required screening system for athletes including ECG screening before each season and a follow-up echocardiogram if an abnormality is detected (Baxter, 2012). International sport governing bodies such as FIFA and the International Olympic Committee also require ECG screening for congenital heart defects. High schools have adopted similar practices to identify at-risk athletes before engaging in high intensity sports, but practical concerns such as cost-effectiveness are an issue (Drezer & Corrado, 2011).

**Cardiovascular Monitoring for ADHD Stimulant Users (RL)**

Like with cardiovascular-stressing sport competitions, there has also been much debate over whether patients being prescribed ADHD stimulants should first have to be screened and cleared using electrocardiography. Recently, the American Heart Association (AHA) released a statement suggesting that ECGs should routinely be given to children prior to starting stimulant therapy to treat ADHD (Perrin, 451). This way, potential abnormalities could be detected, and FDA warnings could be followed. If ECGs presented structural damages or some example of cardiac dysfunction, the AHA argued that the patient would be put at risk according to FDA recommendations. Opposing organizations like the American Academy of Pediatrics (AAP) argued that their own evidence suggested that ECG screening was not an effective solution. Considering the very rare circumstances in which an individual suffers sudden cardiac death, there was no significant difference in the rate of occurrence of SCD in ADHD-medication users versus non-users (Perrin, 452). The two groups came to agreement on the fact that no scientific evidence suggested ECG screening would prevent SCD (Perrin, 452).

While many organizations, including the AHA and AAP, believe the ADHD stimulant medication warnings by the FDA should be taken seriously, no evidence to date supports the institution of laws mandating ECG screening for future ADHD medication users. It has been deemed that ECG screening does not have a balance of benefits, risk, and cost-effectiveness when considering the insignificant differences between rate of SCD in stimulant users and non-users (Perrin, 452).
A number of studies have examined whether significant difference exists between the occurrence of cardiovascular events in ADHD stimulant users and non-users. In 2011, Cooper et al. investigated the issue at hand. Using information from four large health plans, they were able to split the population into ADHD medication users and non-users. It was determined that within the population, significant cardiac events occurred at a rate of 3.1 per 100,000 person-year (Cooper et al., 1901). That equated to a couple thousand incidents each year for the American population. Additionally, ADHD medication users were no more susceptible to such cardiovascular events as non-users. These results were mirrored in additional studies. In 2011, Schelleman et al. reported that although case studies of SCD appear numerous, no conclusive evidence has shown that such an event is more prevalent in ADHD stimulant users than non-users. Winterstein et al. echoed the same sentiments in a smaller study performed in 2007. Examining cardiac hospital admissions, her group stated that available case studies of SCD were not representative of the risk/non-risk associated with ADHD stimulants.

**Linking ADHD Medication Use, Exercise, and Cardiovascular Events (CM, MM)**

Case studies linking ADHD stimulant use to cardiac events in sports is a more daunting research task. The case studies previously mentioned illustrate how high intensity activity in sport can be detrimental to the cardiovascular system. Paired high intensity activity, stimulant use can further aggravate existing heart conditions. For example, in 2006, the U.S. Food and Drug Administration reviewed Adderall and its effects and found that a 12 year old girl died while running, after being on the drug for five months (Ireland, 2011). Research further indicated that death may have been partially attributed to a genetic heart condition (Ireland, 2011).

Another case included a 15 year old male who suffered a myocardial infarction after being prescribed Adderall XR 5mg by his doctor four days prior. The male came to the hospital with sudden severe headaches and chest pain. Although his vital signs appeared fine, the Adderall XR acted as a vasoconstrictor, diminishing the amount of blood being pumped throughout systemic circulation (Agarwala et al. 2011). This would undoubtedly pose an issue if the patient were to participate in high intensity activity, and EKG screening may be warranted in the future.

According to the Journal of the American Academy of Pediatrics, the risk of cardiovascular effects and sudden death in individuals using ADHD medication and individuals not using ADHD medication is the same (Biederman 2006). There was no correlation seen between the two groups. In fact, higher risk of damage to the cardiovascular system was only found in individuals who had a pre-existing heart defect. To provide further evidence, the Journal of Pediatrics conducted a study of 2,000 individuals and compared the cardiovascular effects of patients being treated with ADHD medication with those effects in patients who were not using ADHD medication at two years and six years after the start of the study (Biederman et al. 2006). The results indicated that after two years, there was only a slight increase in blood pressure and heart rate, but after the six year follow-up no changes were seen among the two groups; the
patients treated with ADHD medications maintained average blood pressure and heart rate levels thereafter.

Another case study involved 14 boys who had been diagnosed with ADHD and had been taking a methylphenidate or amphetamine for six months or longer (Cole et al. 2008). The study was focused on the measurement and analysis of aerobic responses from the group when performing cardiovascular exercise. The exercise program involved the use of stationary bicycles and treadmills, and aerobic exercise was performed at twenty-minute intervals (Cole et al. 2008). The results indicated that boys diagnosed with ADHD had a higher work capacity, and due to the effects of their ADHD medication, used less energy than their non-ADHD diagnosed counterparts.

Although there is little correlation with the effects of ADHD medications in accordance with cardiovascular side effects and sudden death, there is supporting evidence that ADHD medications can be used to enhance the performance of athletes in sporting competition. A recent case study involved six college athletes in a sporting competition. Each was prescribed 10mg of adderall to measure any subsequent performance enhancement (Factor et al. 2010). Two hours after taking the medication, researchers saw positive effects on the athletes’ performance including increased strength, increased acceleration, increased anaerobic capacity, and decreased fatigue (Factor et al. 2010). Another case study concluded that eight male athletes saw improved performance in extreme climate conditions, including excessive heat, after taking a methylphenidate, than the control group of athletes prescribed a placebo (Factor et al., 2010).

**Prevalence of ADHD Among Professional Athletes (MM)**

Among professional and college athletes, all medications that are being taken must be prescribed by a physician and have proper documentation. Since ADHD medications can be classified as stimulants, the NFL, NCAA, and other sporting leagues have banned their usage unless athletes are prescribed (NCAA 2012). As of August 1st, 2009, the NCAA made the Medication Exception Policy even stricter, adding that athletes being prescribed ADHD medications with proper documentation must also have a clinical assessment done (NCAA 2012). Although these organizations apply these rules, the NCAA’s most recent drug survey reveals that 4.3 percent of students-athletes use stimulants with a prescription while 6.3 percent take the stimulants without a prescription (Hendrickson 2012). In the NFL, some players have been suspended from games due to positive tests of amphetamines found in their systems. Even with the NFL ban on ADHD medications and the NCAA’s stricter policy, the prevalence of ADHD medications in sports is still an issue because many athletes taking the medication without being prescribed still exceeds the athletes who are prescribed and have the necessary documentation. Injuries and deaths from athletes taking ADHD medications is not readily available to the public due to confidentiality, but with the help of a physician, additional findings may result.
**Discussion and Solutions** (CM, RL, MM)

After a review of the current literature on the topic of ADHD medication and its effects on physiological risk, little was found suggesting plausible solutions to the issue. However, research was mixed on whether these medications were, in fact, causing cardiovascular events that, otherwise, would not occur if not for the medication. This can suggest that a problem may not actually exist.

Although there is not enough information suggesting how the drug can negatively affect individuals, as well as little correlation between the effects of cardiovascular events among individuals taking and not taking these stimulants, there maintains evidence that it can increase performance as seen in the case studies. Because of the lack of research in this field, users of ADHD medication to improve performance should be aware of the FDA warning issued on these medications and expect that side effects may occur.

Problems may arise when ADHD medications are taken in conjunction with bouts of exercise. The seemingly low risks associated with such pharmaceutical drugs become much more magnified as intensity of physical activity increases. Within the general population, anywhere from 10-25% of SCDs are related to physical exertion (Liberthson, 1043). Physical activity acts as a stressor to the human body, and many research studies have shown how exercise influences the neuroendocrine system (Hackney, 2006). Increased circulation of hormones, like the aforementioned catecholamines, enable the body to deal with the stresses of exercise. These responses become exacerbated as both intensity and duration of physical activity increases (Hackney, 2006). Therefore, physical activity in combination with ADHD medication, especially at high intensity (e.g. competing in a sporting event), has the potential to completely overload the system to produce harmful consequences.

In previous sections, the similarities between the physiological effects of both ADHD medication and exercise have been discussed. Each were shown to positively affect the human brain due, in part, to increases in circulating catecholamines. When physical activity is performed in combination with the intake of such medication, it is postulated that an overabundance of circulating catecholamines can exist within the body. The higher-than-normal levels of catecholamines are indicative of very high-intensity physical activity. The body begins to work harder than actually required, as circulating hormone levels give the perception of increased work. Heart rate, respiratory rate, and blood pressure can all increase mightily. Thus, it is hypothesized that performing high-intensity physical activity, like that observed when participating in sports, can be particularly dangerous when done so in conjunction with ADHD medication intake.

It may, therefore, be worthwhile to examine how many cardiovascular events can actually be attributed to the intake of ADHD medications. While exact numbers may be difficult to obtain
as other factors beside medications may have caused such disturbances, it may be possible to look at hospital patients with both cardiovascular events (e.g. arrhythmias, heart attacks) and circulating ADHD medication at time of admittance. Local hospitals may provide anonymous medical records that would potentially reveal a correlation between ADHD medication use and cardiovascular disturbances. Like previous studies before, this may not produce a significant distinction between cardiovascular events in ADHD stimulant users and non-users. It may be worthwhile to continue work mentioned by organizations like the American Heart Association. Perhaps, instead of using ECG to screen every potential ADHD medication user, it may be more beneficial and cost-effective to screen only those with family or personal history of cardiovascular events (e.g. arrhythmias, myocardial infarct).

In addition, an initiative to halt ADHD medication misuse for exercisers and athletes may prove beneficial. A survey of the college community at Rutgers University may provide insight into the prevalence of medication misuse among students. Furthermore, data concerning the number of people who perform physical activity while on such drugs may present itself. Together, the research could be used to get the word out to the representative community. Distributed pamphlets could teach future ADHD drug users of the potential risks associated with exercising under the influence of such medications. As another solution, since there is little information, awareness and prevention can be good solutions to get news out to the public. Also, to provide attention to this issue, letters to a “higher authority”, the American Medical Association, research institutions and the government can also help increase the awareness. The more information and research that can be done this issue can be of great use to the public for them to understand how taking ADHD and other medications that is usually prescribed for a certain diagnosis can have on the body.
Community Action: The Assisted Medical Record Examination of Cardiac Events in Sports (RL)

In relatively few studies, it has been shown that no significant difference exists in the occurrence of cardiovascular events in ADHD stimulant users and non-users. However, those studies do not take into account stimulant users under physiological stressors such as exercise. Reports of sudden cardiac death and other cardiovascular disturbances in a sport setting also raise an area of concern. It is unknown whether such tragedies are the result of combining stimulant medication with physical activity.

In order to determine whether there is a possible link between cardiac events in sports and stimulant medications, we have proposed examining medical records for any individual treated for a cardiovascular disturbance during exercise. Once said individuals are discovered within the records, information on substances within the body at the time of admission can determined. A similar process can be done for those who lost lives during a sporting event. By looking at the rate of stimulant use in individuals suffering cardiac events, we can determine whether a correlation between the two actually exists.

Besides being able to share this information with the public, a correlation between stimulant use and physical activity could have large implications in the ways doctors prescribe ADHD stimulants. If, in fact, the examination of medical records yields significant findings, organizations like the American Heart Association may have enough evidence that would lead to the creation of guidelines requiring ECG screening prior to being prescribed ADHD stimulants. Additionally, this might actually help to alleviate some of the abuse surrounding ADHD drugs. Individuals may be less willing to go to doctors asking for such prescriptions if they are forced to pay for an ECG prior to obtaining the drugs.

Considering our status as undergraduate researchers, it will not be possible to gain access to the medical records that we will need to answer such a question. Instead, we have called upon three large organizations for help. We have written a letter to the American Medical Association (AMA), the Food and Drug Administration (FDA), and the Drug Enforcement Administration (DEA) to request that they look into whether a correlation exists between cardiac events and exercise while on ADHD medications.

The letter sent to the American Medical Association (AMA), the Food and Drug Administration (FDA), and the Drug Enforcement Administration (DEA) is as follows:

American Medical Association
515 N. State Street
Chicago, IL 60654
(800) 621-8335
To Whom It May Concern:

We are writing as a group of students from the School of Environmental and Biological Sciences at Rutgers, The State University of New Jersey. Under the tutelage of Dr. Julie Fagan, the group hopes to present to your organization what may be a current problem, in the hopes that you will investigate it further.

Attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed psychiatric disorder in children. Additionally, it is now known that more than 50% of diagnosed children continue to experience symptoms into adolescence and adulthood. Currently no single etiology exists for ADHD, but a growing body of research has shown deficits in attentional regulation within the prefrontal cortex of the brain as a major contributor to ADHD onset. Furthermore, research has indicated that dysregulation of catecholamine circuits within the prefrontal cortex has shown to have a major influence on the prevalence of ADHD. Many forms of treatment, particularly stimulant medication (e.g. Adderall), attempt to correct such catecholamine dysfunction. However, as with any pharmaceuticals, positive outcomes may come at the risk of negative side effects. Specifically, we believe that the aforementioned catecholamine response, as affected by stimulant medication, may become exacerbated under certain physiologically stressing circumstances (i.e. intense physical activity).

Through the remainder of this letter, we hope to (1) establish that a hole in the scientific literature connecting ADHD stimulant medication and cardiovascular events exists, (2) ask your organization to utilize its resources to gather statistics to help answer the problem at hand, and (3) promote possible change in protocol for physicians administering ADHD drugs.
The public is always dumbfounded at how innocent young lives can be lost suddenly in locations such as a football field or basketball court. Each year, numerous cases of sudden cardiac death (SCD) contribute to the leading cause of death in young athletes. No evidence to date has been able to form a prediction method for determining who may be at risk for sudden cardiac death. We propose that there may be a link between the intensity of sport competition and the use of stimulant medications.

Attention-deficit/hyperactivity disorder stimulants, like Adderall, are commonly misused as a sport performance enhancer. It is for that reason that organizations, like the National Collegiate Athletic Association (NCAA), National Football League (NFL), and Major League Baseball (MLB) require notes from physicians stating the athlete has been prescribed such drugs. Regardless, athletes continue to take the stimulant drugs (some without a prescription), which alter the catecholamine response and can increase stroke volume and cardiac output of the heart, decrease perceived exertion, and increase heart rate. This is all occurring at the same time as high-intensity competition or exercise, which promote similar increases in cardiovascular function. Together, the two may combine to exacerbate the effects of catecholamine response on the cardiovascular system.

Additionally, there is debate over whether individuals prescribed ADHD stimulants should first have to be screened using electrocardiography. Stimulants currently have labels that instruct individuals with structural heart conditions or pre-existing cardiovascular disturbances to not take such medication. Also, medication guides, distributed every time an ADHD stimulant prescription is filled, warn that sudden death has occurred in individuals with such pre-existing conditions or poor family history. The American Heart Association has been a supporter of ECG screening prior starting stimulant therapy to treat ADHD. If ECGs presented structural damages or some example of cardiac dysfunction, the AHA argued that the patient would be put at risk according to FDA recommendations. Since that statement, a few studies have demonstrated that there has been no observed significant difference between the prevalence of cardiac events in stimulant users and non-users. However, no such study has examined such numbers in the context of athletes during competition.

We hope that your organization will consider collecting such data. It is proposed that access to medical records and their subsequent examination may lead to a correlation between stimulant use and sudden cardiac death. Firstly, it would be essential to examine all known cases of sudden cardiac death or cardiac events occurring during a sporting event. From those select cases, it can then be examined whether the athletes who experienced such events had circulating levels of ADHD medications. A correlation between the two can then be established. Our group has limited access to such data, but we hope that your organization can help bring our project to fruition.
Besides the fact that this would greatly extend scientific literature in the field, it would also promote general awareness about using stimulant medication under the rigors or physical activity. Additionally, if a correlation is deemed to exist, this may lead to mandates concerning ECG screening. It may prompt physicians to screen for cardiovascular abnormalities prior to prescribing ADHD medication. Furthermore, if new mandates resulted from the research into medical records, it may help to combat some of the abuse surrounding ADHD stimulant use. For example, required ECG screening may deter an individual without ADHD from simply going to the doctor’s office, demonstrating symptoms of the disorder, and then asking for such a prescription.

We hope that your organization realizes the importance of this issue and will seek to further investigate the potential risks of physical exertion while taking ADHD medications. If such a link was found, it would be hoped that guidelines would be instituted that might require ordering an ECG prior to the prescription of ADHD medications.

Sincerely,

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References


NCAA. 2012. Medication Exception Ban


Appendix 1

Table 1: The Official 2010 TCPR ADHD Medication Comparison Chart

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose (starting-max)</th>
<th>Available Strengths (in mg except where noted)</th>
<th>Duration of Action</th>
<th>Can it be Split?</th>
<th>Generic Available?</th>
<th>Ages Approved for ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methylphenidates</strong></td>
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<tr>
<td>Short-acting</td>
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</tr>
<tr>
<td>Ritalin</td>
<td>5 mg BID-20 mg TID</td>
<td>5, 10, 20</td>
<td>3-4 h</td>
<td>yes</td>
<td>yes</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Focalin (dexamethasone)</td>
<td>2.5 mg BID-10 mg BID</td>
<td>2.5, 5, 10</td>
<td>3-4 h</td>
<td>yes</td>
<td>no</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Methylin</td>
<td>5 mg BID-20 mg TID</td>
<td>5, 10, 20</td>
<td>3-4 h</td>
<td>no</td>
<td>no</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Methylin CT</td>
<td>5 mg BID-20 mg TID</td>
<td>2.5, 5, 10</td>
<td>3-4 h</td>
<td>no</td>
<td>no</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Methylin Oral Solution</td>
<td>5 mg BID-30 mg BID</td>
<td>5 mg/5 ml, 10 mg/5 ml</td>
<td>3-4 h</td>
<td>NA</td>
<td>no</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Intermediate-acting</td>
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<tr>
<td>Ritalin SR</td>
<td>10 mg q AM-60 mg q AM</td>
<td>20</td>
<td>4-8 h</td>
<td>no</td>
<td>yes</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Metadate ER</td>
<td>10 mg q AM-30 mg BID (max 60mg/day)</td>
<td>10, 20</td>
<td>6-8 h</td>
<td>no</td>
<td>no</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Methylin ER</td>
<td>20 mg q AM-60 mg q AM</td>
<td>10, 20</td>
<td>4-8 h</td>
<td>no</td>
<td>no</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Long-acting</td>
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<tr>
<td>Concerta</td>
<td>18 mg q AM-72 mg q AM (if 12+ y.o.)</td>
<td>18, 27, 36, 54</td>
<td>10-16 h</td>
<td>no</td>
<td>no</td>
<td>6-12: up to 54 mg, 12+: up to 72 mg</td>
</tr>
<tr>
<td>Daytrana (methylphenidate nasal spray)</td>
<td>10-30 mg q AM. Remove after 9 hours</td>
<td>10, 15, 20, 30</td>
<td>8-12 h</td>
<td>no</td>
<td>no</td>
<td>6-12 only</td>
</tr>
<tr>
<td>Focalin XR (dexamethasone XR)</td>
<td>6-17: 5 mg q AM-30 mg q AM; adults: 10 mg q AM-45 mg q AM</td>
<td>5, 10, 15, 20, 30</td>
<td>8-12 h</td>
<td>no</td>
<td>no</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Metadate CD</td>
<td>20-60 mg q AM</td>
<td>10, 20, 30, 40, 50, 60</td>
<td>9-12 h</td>
<td>can be sprinkled; do not crush or chew</td>
<td>no</td>
<td>6+</td>
</tr>
<tr>
<td>Ritalin LA</td>
<td>20-60 mg q AM</td>
<td>10, 20, 30, 40</td>
<td>8-12 h</td>
<td>no</td>
<td>no</td>
<td>6+</td>
</tr>
<tr>
<td>Amphetamines</td>
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<tr>
<td>Short-acting</td>
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</tr>
<tr>
<td>Dexedrine (dextroamphetamine)</td>
<td>3-5: 2.5mg qAM-20 mg BID; 5-16: 5 mg q AM-20 mg BID</td>
<td>5, 10</td>
<td>3-5 h</td>
<td>yes</td>
<td>branded generic of Dextroamphetamine</td>
<td>3-16</td>
</tr>
<tr>
<td>Lisdex (Dextroamphetamine)</td>
<td>5-20mg BID</td>
<td>5 mg/5 ml</td>
<td>3-6 h</td>
<td>no</td>
<td>no</td>
<td>3-16</td>
</tr>
<tr>
<td>Dexoxyn (methamphetamine)</td>
<td>5 mg q AM-10 mg BID</td>
<td>5</td>
<td>3-6 h</td>
<td>yes</td>
<td>yes</td>
<td>6-17, adults</td>
</tr>
<tr>
<td>Intermediate-acting</td>
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<td></td>
</tr>
<tr>
<td>Adderall</td>
<td>5-30 mg BID or 5-60 mg q AM</td>
<td>5, 7, 10, 12, 15, 18, 20, 30</td>
<td>4-8 h</td>
<td>can be crushed</td>
<td>yes</td>
<td>3+</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexedrine Spansules (dextroamphetamine)</td>
<td>5 mg q AM-20 mg BID</td>
<td>5, 10, 15</td>
<td>10-14 h</td>
<td>no</td>
<td>no</td>
<td>6+</td>
</tr>
<tr>
<td>Adderall XR</td>
<td>5 mg q AM-40 mg q AM</td>
<td>5, 10, 15, 20, 25, 30</td>
<td>8-12 h</td>
<td>can be sprinkled; do not crush or chew</td>
<td>yes</td>
<td>6+</td>
</tr>
<tr>
<td>Vyvanse (methylamphetamine)</td>
<td>30 mg q AM-70 mg q AM</td>
<td>20, 30, 40, 50, 60, 70</td>
<td>8-12 hrs</td>
<td>Can be dissolved in water</td>
<td>no</td>
<td>6-12, adults</td>
</tr>
</tbody>
</table>
### Appendix 2

#### Table 2: Side effects for ADHD Medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approved Age</th>
<th>Common Side Effects</th>
<th>Duration of Behavioral Effects</th>
<th>Pros</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritalin® Methylphenidate</td>
<td>6 and older</td>
<td>Insomnia, decreased appetite, weight loss, headache, irritability, stomach ache</td>
<td>3-6 hrs</td>
<td>Works quickly (within 30-60 minutes); effective in over 70% of patients; good safety record</td>
<td>Not recommended in patients with marked anxiety, motor tics, or with family history of Tourette's Syndrome</td>
</tr>
<tr>
<td>Ritalin SR® Methylphenidate (Extended Release)</td>
<td>6 and older</td>
<td>Insomnia, decreased appetite, weight loss, headache, irritability, stomach ache</td>
<td>7 hrs</td>
<td>Particularly useful for adolescents with ADHD to avoid nighttime dose; good safety record</td>
<td>Slow onset of action (1-2 hours); use cautiously in patients with marked anxiety, motor tics, or with family history of Tourette's Syndrome</td>
</tr>
<tr>
<td>Dexedrine® Dextroamphetamine</td>
<td>3 and older</td>
<td>Insomnia, decreased appetite, weight loss, headache, irritability, stomach ache</td>
<td>3-6 hrs (table); 7-10 hrs (capsule)</td>
<td>Works quickly (within 20-60 mins); may retard somewhat longer than other standard stimulants</td>
<td>Use cautiously in patients with marked anxiety, motor tics, or with family history of Tourette's Syndrome</td>
</tr>
<tr>
<td>Adderall® Amphetamine</td>
<td>3 and older</td>
<td>Insomnia, decreased appetite, weight loss, headache, irritability, stomach ache</td>
<td>3-6 hrs</td>
<td>Works quickly (within 20-60 mins); action may last somewhat longer than other standard stimulants</td>
<td>Use cautiously in patients with marked anxiety, motor tics, or with family history of Tourette's Syndrome</td>
</tr>
<tr>
<td>Concerta® Metadate</td>
<td>6 and older</td>
<td>Insomnia, agitation, headache, irritability, stomach ache, infrequent abnormal liver function tests have been reported</td>
<td>12-24 hrs</td>
<td>Given only once a day</td>
<td>Maintain 2-4 weeks for clinical response; regular blood tests needed to check liver function. Because of this, it is not recommended as first line drug therapy for ADHD</td>
</tr>
</tbody>
</table>
Dear Editor of The Daily Targum,
Please consider publishing our letter below (and attached).

I wanted to share with the Rutgers community an issue that does not receive much attention and has the potential to detriment students’ health. Many students and student-athletes are prescribed stimulants to mitigate inattentiveness and other symptoms commonly associated with Attention Deficit Hyperactivity Disorder (ADHD). Knowing what we know about the stress that exercise and sports put on the human body, Rutgers University professor Dr. Julie Fagan and researchers, including myself, hypothesize that when paired with high intensity cardiovascular exercise, ADHD stimulants such as Adderall, may exacerbate the cardiovascular system. If this proves to be true, students taking these medications who participate in high intensity aerobic exercise or sport may be at increased risk for cardiovascular events, such as a heart attack or sudden death. Our literature review, titled “ADHD Medication and Exercise: The Combination’s Implications of Sport Safety” further explores this proposal.

Currently, there is little information linking ADHD medication, high intensity exercise, and cardiovascular events. A connection, however, exists between ADHD medication and cardiovascular dysfunction, only when a pre-existing heart condition is present. Laws mandating electrocardiogram screening exist when entering a professional sport league, such as Major League Soccer, but EKG screening for patients prescribed ADHD stimulants is currently been a topic of much debate. If EKG screening practices were routine, heart abnormalities could be better-detected and cardiovascular events in sports and exercise could be prevented.

Considering all of this, a potential solution is to increase awareness of these issues in a public forum. Misuse of ADHD medication is rampant throughout the college campus, and when paired with exercise, we may see a growing number of tragic physiological occurrences.

Please look out for our research project, which will be published online this summer.

Thank you,
Christen Morrison
Rutgers University Class of 2013, School of Environmental and Biological Sciences, Exercise Science Major
Dear Editors of Scientific American,
Please consider publishing this idea below (and attached). Thank you for your time.

Sincerely,
Ryan Lavell
Rutgers University Class of 2013, School of Environmental and Biological Sciences, Exercise Science Major

I wanted to share an issue that has direct implications to many unsuspecting individuals. Attention-deficit/hyperactivity disorder (ADHD) is a growing diagnosis across the United States, and in most cases, stimulant medications are used to combat the disorder. These medications, which are proposed to correct catecholamine dysfunction in areas of the brain controlling attention, also create possible cardiovascular risks. In 2006, The Food and Drug Administration (FDA) acknowledged those risks and issued changes to labels warning of such side-effects. Additionally, medication guides are issued each time a patient is prescribed, and subsequently fills, ADHD medications. The guides warn that sudden death has occurred in individuals with pre-existing heart conditions and/or family history of cardiac abnormalities and disease.

As a member of a research team at Rutgers University under the guidance of Dr. Julie Fagan, we are concerned that unexplored cardiovascular conditions can prompt sudden cardiac death (SCD) in individuals taking ADHD medications. Particularly, we worry that exercise and sport competition, which similarly affects the catecholamine response as seen with ADHD stimulants, may overload the cardiovascular system. It is hypothesized that the combined catecholamine effect may exacerbate the cardiovascular system, specifically in warned individuals with pre-existing heart conditions or family history.

There is a growing debate as to whether patients being prescribed ADHD stimulants should first be screened and cleared using electrocardiograms (ECG). The American Heart Association (AHA) released a statement that advised children to be screened using ECG prior to starting stimulant therapy. If the ECG revealed structural damages or abnormalities, the AHA argued that the individual would be put at risk according to FDA recommendations. Most scientific research to date has demonstrated no significant differences between the occurrences of cardiac events (e.g. myocardial infarct, heart palpitations) between ADHD stimulant users and non-users. This, among other evidence, has caused the AHA to rescind their statement. It was declared that the benefits of ECG screening did not outweigh the risks and costs when considering the lack of evidence for significant differences between groups.
Regardless, instances of sudden cardiac death in sports present themselves each year; emotional stories of athletes dying on the field are established. We hope to help propose a solution to such a problem by discovering whether such catastrophes are the product of stimulant medications and our hypothesized physiological mechanism. We urge physicians and those researching medical records to assist the situation by helping us determine whether cardiac events in athletes are occurring while under the influence of stimulant medications. It is then that we might be able to propose proper mandates on ECG screening with ADHD medication.
Dear Editor of the South Jersey Times,

My name is Mabel Majekodunmi and I would like to bring your attention to a concerning matter that has the potential to bring harmful effects to users. The improper usage of ADHD, attention deficit hyperactive disorder, medications as performance enhancers in exercise can increase the risk of cardiovascular effects in individuals who are taking the medication without a prescription and for recreational use. ADHD medications are known to increase the heart rate and blood pressure of an individual, taking these medications while exercising has the potential to produce many side effects because aerobic activity also increases the heart rate and blood pressure. With my fellow researchers along with our supervisor, Dr. Julie Fagan, we have came up with a literature review that looks into the implications of sport safety with ADHD medication and exercise.

Since this is a new area, there is not much research and known findings on this particular topic and also not enough information about the correlation between ADHD medication and exercise with cardiovascular risk. The awareness of this issue must be available to individuals who do not understand the effects of these medication because people taking ADHD medications without a prescription although rare can are increasing risk for cardiac arrest and other heart defects.

A comprehensive review will be published online in the summer.

Sincerely,
Mabel Majekodunmi
Biological Sciences Major
SEBS, Rutgers University
Class of 2013