Official Title: Effect of Docosahexaenoic Acid (DHA) and Eicosapentaenoic Acid (EPA) on Brain Executive Function in Student Athletes
NCT04570995
IRB-Approved Date: 10/29/2020

Wake Forest®
School of Medicine

Effect of Docosahexaenoic Acid (DHA) and Eicosapentaenoic acid (EPA) on Brain Executive Function in Student Athletes

Informed Consent to Participate in Research
Elaheh Rahbar PhD, Principal Investigator

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are an active student athlete on the Wake Forest University baseball squad. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask the study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to determine if daily oral intake of an encapsulated fish oil supplement (containing docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)) can improve important mental skills (for example: attention, problem solving, moral reasoning, decision-making; collectively called brain executive function) in collegiate baseball student athletes over a course of an academic school year.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Thirty-five to forty people at this research site will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

If you agree to participate in this study, you will be randomized to one of two study groups based on the type of dietary supplement consumed. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in each oil group. One group will consume fish oil capsules and the other group will consume a placebo capsule (containing safflower oil; a common cooking oil).

Neither you nor the investigator or the study staff will know which study oil you are receiving at any time during the study. This is done so that a fair evaluation of results can be made. However, this information can be retrieved by the researchers if needed in the case an emergency situation.

Study Overview

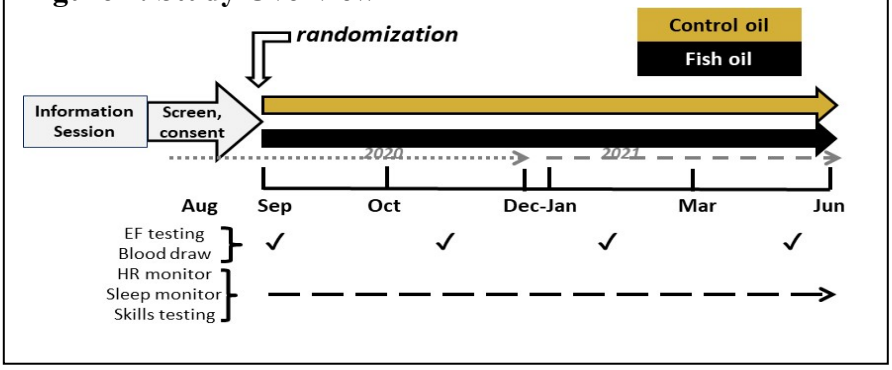
Figure 1 shows the design of the study over the course of the 2020-21 academic year and baseball season. You will be introduced to the study at an Information Session (early October~~late September~~). If you would like to participate, we will then review the consent form with you in a confidential manner. Once you agree to participate by signing the consent form, you will be

randomized to one of the two study arms and consume the study-provided dirty oil capsules for the entire academic year. There will be four (4) fasting study visits over the course of the academic year to which you will come. We will draw a small volume of blood at these study visits and ask to complete a number of executive function (EF) tests, as described below in more detail.

Study Details

Once you agree to participate by signing the consent form, we will collect medical history information and evaluate your eligibility for the study. At this visit, we will also make some body measurements (height, weight, waist & hip circumferences) and ask you to complete some surveys to tell us about your typical diet, cognitive abilities and mental status (**Table 1**).

Figure 1: Study Overview



Once enrolled and randomized to a study arm, you will be asked to come to the David R. Couch Baseball Park facility on a daily basis (5 days/week) to consume (onsite with a snack) your assigned study-provided dietary oil capsules (2 softgel capsules/day; ~2 g oil/day). The Athlete Department Nutritionist will monitor your daily consumption of the dietary supplement. You will receive a weekly call from the study staff to assess your compliance as well. As mentioned above, neither you nor the study staff will know which study oil you are taking. The two types of encapsulated oils are identical in appearance and you should not exchange capsules with your teammates who are also participating in the study.

You will be required to consume your study-provided dietary oil capsules for the entire academic year. During school breaks, holidays and baseball season travel, you will be provided with enough oil capsules to consume while you are away from campus. You will be asked to maintain a log of dietary supplement consumption during your time away from campus.

On four (4) occasions over the academic year (see Figure 1; early October, mid November, early February, and mid-May), we will ask you to come to the Baseball Park facility in the early morning after an overnight (8 hour) fast. At each of these morning (7am-9am) fasting study visits, you will check-in and we will ask you about your general health, review your study-provided dietary oil capsule consumption, ask about your diet, use of pain relievers and tobacco, and about any sports-related injuries. We will make some body measurements (weight, waist & hip circumference). You will have approximately 20 milliliters (~4.1 teaspoons) of blood drawn from a vein in your arm at each of the four fasting study visits by a trained nurse and/or phlebotomist. The blood will used to measure some key biomarkers related to inflammation, specifically hsCRP, cortisol, and two inflammatory biomarkers (interluekin-6 and TNFa). These are values frequently requested by family physicians to verify a person's health, but we are doing these for research purposes. From a portion of your Visit 2 blood sample, we will isolate DNA

in order to determine your genotype at a single gene variant that we have observed to regulate metabolism of the study oils in the dietary supplements that you will be consuming. We will also measure the fat content of your plasma and your red blood cells. This is for research purposes and will show us how the fats are being processed by your body.

After eating a snack provided by the Baseball Park facility Nutrition Center, we will ask you to complete a couple of surveys and then take a battery of computer-based executive function (EF) tests in a quiet room at visits 2-5. The fasting visits (V2-V5) will have the same structure as shown in Table 1.

Table 1: Study Activities by Visit and Duration of Tasks

Task	*Estimated time*	*Pre-visit screening*	*Visit 1*	*Visit 2*	*Visit 3*	*Visit 4*	*Visit 5*
Informed consent	15m	X					
Medical History, Inclusion/Exclusion criteria	15m	X					
Baseline surveys	~1.5hr	X					
Enrollment	n/a	X					
		X					
Wellness assessment	5m	X	X	X	X	X	X
Anthropomorphic measurements	5m	X	X	X	X	X	X
Blood collection	15m		X	X	X	X	X
Executive Function tests	~45min		X	X	X	X	X
Lab/Blood Chemistries	n/a		X	X	X	X	X

Randomization will be performed by the biostatistician after enrollment. The stated **Time** is an approximation of the time necessary to complete the indicated Task.

We can give copies of your blood test results to you to give to your personal physician, if you choose. We will, however, not share the test results with anyone. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study.

Other Data Collection

To help monitor your health and improve your skills, your baseball coaching team collects a variety of data of their student athletes as part of their personalized training approach. Your coaching team has assigned you a wrist band monitor (WHOOP strap) to monitor your health and wellness. As part of your training system, the coaching team utilizes a premier system (DynaVision) to re-enforce attention, reaction time, hand-eye coordination, balance and cognitive processing skills. They also use an Adaptive Capacity testing system to better understand a student athlete's thinking process, reactional tendency and learning mode. Each of these data systems aligns very well with the goal of this study to understand the impact of dietary supplements executive function and the physiological factors (for example stress, sleep, anxiety) that effect brain activity. Finally, if you incur an injury during the academic season, the team physician will provide your injury metrics to the study team to determine if the dietary fish oil helped with your recovery and/or return to play.

The coaching team has agreed to share the data they collect with the study team in order to greatly enhance the potential outcomes of this study. We ask for your permission for the coaching team to share the described data with the study team. I agree to share these data with the study team:

[ ] Yes, I'm willing to share ALL of my data.

[ ] Yes, I'm willing to share some of my data. Select those you want to share below.

[ ] WHOOP data. [ ] Adaptive Capacity data.

[ ] DynaVision data. [ ] Injury-related data.

[ ] No, I'm NOT willing to share ANY of my data. _____ Initials

Storage of Biological Tissue

If you agree to participate in this study, we will draw approximately a total of 100 milliliters of blood over the entire study period (~20 mL per visit). Most of these samples will be used immediately but any remaining sample will be kept and may be used in future research to learn more about other conditions. Your sample will be obtained at the David R. Couch Baseball Park facility by a study team member experienced in drawing blood (e.g. nurse/phlebotomist). The sample will be stored in the laboratory of Dr. Rahbar at the Wake Forest School of Medicine and it will be given only to researchers approved by Dr. Rahbar. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. In order to participate in this study, you must be willing to provide this sample for future research. I agree that my blood samples can be stored for future use:

[ ] Yes [ ] No _____ Initials

Your blood/tissue samples, EF data, and all other biometric and survey data, will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name and contact information, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

In the future, research on your specimen may involve whole genome sequencing or genotyping of genetic variants. You can choose to opt out of all genetic testing, below.

[ ] Yes, I provide full consent for future genetic testing

[ ] No, I do not want any genetic testing _____ Initials

The research that may be performed with your blood samples is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might benefit people and student athletes at some point in the future, but it is not known if this will happen. The results of the research performed with your blood and EF data will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood/tissue samples and EF data will not affect your care.

Your blood samples and EF data will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about 9 months, beginning at the start of the 2020-21 academic year and ending with the close of the Spring academic semester (May 2021).

You participation is voluntary. You can stop participating at any time. If you decide to stop participating in the study, we encourage you to talk to the study team first to learn about any potential health or safety consequences.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. The most likely side effects related to the dietary oils we are studying include are possible gastrointestinal upset at the beginning of the oil supplementation period due to your body not being used to consuming oils. This can be minimized by taking the encapsulated oils with food.

You may experience discomfort, bruising and/or bleeding where the needle is inserted into your arm for blood draws. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia). If you donate blood to the American Red Cross, you should talk with the study doctor about whether or not it is safe to do so while participating in this study. You should not donate blood more than 2 times per week and no more than approximately one pint (about 500 ml) of blood in an eight week period.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

The risk of harm or discomfort that may happen as a result of taking part in this research study is not expected to be more than in daily life or from routine physical examinations or tests. You

should discuss the risk of being in this study with the study staff.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study.

Reproductive Risks and other Issues to Participating in Research

Pregnant and lactating women are excluded from participation in this study since they are not among the target population for this study. Both study oil products are available to the general public as cooking oil (safflower oil) or as an over-the counter dietary supplement (fish oil). Both products are generally recognized as safe and have no know reproductive effects in males.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to take the dietary oils. You should talk to your doctor about all the choices you have. Instead of being in this study, you may take the dietary oils over the counter.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your coaching team about your health is considered Protected Health Information. The information we will collect for this research study includes**:** 1. Your identifying information including your name, date of birth, campus address, phone number, and email; 2. The results from your laboratory tests, EF and survey data, and research tests.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee human research studies

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest Baptist Medical Center

3) Our research sponsor, Pharmavite, LLC.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state law.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Rahbar that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Elaheh Rahbar
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but

any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time. Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including any study products and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOU BE PAID FOR PARTICIPATING?

You will not be compensated for your participation in this study.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Pharmavite, LLC (West Hills, CA). The sponsor is providing money or other support to Wake Forest University Baptist Medical Center to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. Elaheh Rahbar, PhD. at [redacted] or after hours at [redacted].

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study team first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

This study will be enrolling student athletes from Wake Forest University. In addition to your rights as a research participant noted in the previous section, as a student, you are under no obligation to participate in this study. You may refuse to participate or withdraw from the study at any time and for any reason without affecting your grades, performance evaluations, or assignments. You will not be pressured into participating in this research study by any statements

or implied statements that your grades, performance evaluations or assignments will be affected by your willingness to enroll in the study. Your medical records/information will not be used by the faculty, administration or study staff to make decisions regarding the status of your medical benefits. If you have questions regarding your enrollment in the study and your status as a student athlete, please contact the Office of Student Services for additional information.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Elaheh Rahbar, PhD. at 3[redacted] after hours at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

Wake Forest®
School of Medicine

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent:_____Date:_____ Time:_____ am pm

Study coordinator verifies complete signatures and dates_____