INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR

Effects of soccer heading on ocular-motor function, brain-derived blood biomarker, and neuronal activity

You are invited to participate in a research study using sensitive tools to detect brain and sensory functions after soccer heading. You were selected as a possible subject because 1) you are a current member of a soccer team who is 18-26 years old and have at least 5 years of soccer heading experience or 2) you are 18-26 years old, have never played organized sports, and have never been diagnosed with a concussion before. Please read this form and ask any questions you may have before agreeing to be in the study.

The study is being conducted by Keisuke Kawata, PhD, ATC, Hannah Block, PhD, Allison Gruber, PhD, Sarah Coon, BS., ATC, Angela Wirsching, BS. ATC.; Indiana University, Department of Kinesiology. Zhongxue Chen, PhD; Indiana University, Department of Epidemiology and Biostatistics. Sharlene Newman, PhD, Isaiah Innis, BS; Indiana University, Department of Psychological and Brain Sciences.

STUDY PURPOSE

Concussion awareness has increased, although subconcussion, which does not produce noticeable signs and/or symptoms, may have the potential to cause neurological dysfunction. However, to this day, we do not know true effects of these minor head impacts. The purpose of this study is to examine if subconcussive head impacts from soccer heading change eye-movement function, brain-derived blood biomarker, and neuronal activity.

NUMBER OF PEOPLE TAKING PART IN THE STUDY

If you agree to participate, you will be one of 80 subjects who will be participating in this research.
We plan to recruit 60 soccer players and 20 non-athlete subjects.

PROCEDURES FOR THE STUDY

For soccer players, if you agree to be in the study, you will be randomly assigned to either a heading, kicking, or standing group.

The study consists of 4 test sessions during a 2-day period. The 1st day will take approximately 4.5 hours. The 2nd day will take approximately 1.5 hours.

- The 1st test session takes place right before the intervention (soccer heading, kicking, or standing).
- You will perform either soccer heading, kicking, or standing intervention.
- The 2nd test session takes place right after the intervention (soccer heading, kicking, or standing).
- The 3rd test session takes place 2h after the intervention (soccer heading, kicking, or standing).
- The 4th test session takes place approximately 24h after the intervention.

During each test session, you will be asked to complete a paper-pencil questionnaire assessing your current feeling. The questionnaire consists of 22 possible symptoms with 7-point Likert scale to detect the presence of concussion-related symptoms and their severity. A certified phlebotomist will draw blood from a vein in your arm at the four time points described in the above paragraph. Each 4ml blood sample is equivalent to approximately 1 teaspoon. A total of approximately 16 ml (3-4 teaspoons) will be drawn during this study. You will be then asked to perform eye-movement tasks using ocular-motor headset. The eye-movement tasks consist of engaging circular target for 15 seconds, and the procedure will be repeated twice. After eye-movement testing, we will measure

your brain activity using either transcranial magnetic stimulation (TMS) or electroencephalography (EEG). The TMS is used to assess brain cells' excitation while you remain seated for 15 mins. TMS works by electromagnetic current that passes through a coil of wire held over the scalp and apply a safe level of electrical current to the brain surface. We will place electrodes on your hand to measure an excitation of the index finger muscle (first dorsal interosseous). You will rarely feel any stimulation from this experiment. The EEG is used to detect brain waves while resting. This experiment is to test basic brain activity, so you will remain seated at least for 10 min. Including preparation of EEG, this experiment will last approximately 30-40 mins. Both TMS and EEG experiments are safe and will not cause any pain.

During the 1st day, in between 1st and 2nd session, you will perform either soccer heading (heading group), soccer kicking (kicking group), or just simply standing while a ball passes over your head (standing group). A standard size 5 soccer ball will be projected at 25 mph (equivalent speed to a long throw-in) by a JUGS soccer machine, and you will perform 10 headers, 10 kicks, or 10 stands, depending on what group you are assigned to. If you are in the heading or kicking group, you will be asked to direct the ball back towards the JUGS soccer machine in the air. If you are in the standing group, you just need to stand still while the ball passes over your head. You will have a 1 min rest between each performance.

RISKS OF TAKING PART IN THE STUDY

While on the study, the risks are:

During soccer heading there is a risk of an injury to your face such as laceration, broken nose, or bruising. There is also a risk of eye, nose, or mouth injury. You may experience minimal transient muscle or joint soreness because of the soccer heading. There is a low risk of concussion and experiencing 1 or more concussion-related symptoms during soccer heading. However, as a soccer player, this type of heading task is a fundamental skill, and you are probably regularly performing the headers during practices and games. We believe the risk is low because most of the previous research did not show any facial injury or concussion-related symptoms. If you are diagnosed with a concussion it will disqualify you from participating in future sporting events until you can safely return to play as determined by a physician. If a diagnostic test (such as a CT scan) is needed, it is not part of the research, but rather part of the clinical management possibly suggested by your physician.

During blood draws, it is possible that you may develop a bruise around the needle insertion. To minimize risks a certified phlebotomist will perform the blood draws using single-use needles, tube holders and test tubes. The skin of the antecubital region (where the needle goes in) will be cleaned with alcohol to further reduce the risks of infections. Following each blood draw the participant will remain seated while maintaining direct pressure against the site of the needle insertion. No long-range risks are anticipated from study participation.

While you are performing eye movement tasks, you may experience a headache or dizziness. The test lasts 30 seconds, and you are free to stop whenever you feel any symptoms. During electroencephalography testing, there may be a slight discomfort associated with sitting still in one position for up to 10-20 minutes. You may also experience skin irritability from a gel. Whenever you experience any discomfort or irritability, you can notify a tester to pause or terminate the experiment. During transcranial magnetic stimulation experiment, there is the potential for you to experience an adverse psychological reaction to the stimulation techniques. Although these risks are very rare, the possible side effects reported in the literatures are temporary loss of consciousness, transient headache, neck pain, toothache, and hearing changes. To minimize any risks associated with the stimulation procedure, the experimenter will closely observe you during the protocols and will ask for feedback from you regarding your symptoms and feelings. You are encouraged to alert the staff about any unusual symptoms you may be experiencing.

BENEFITS OF TAKING PART IN THE STUDY

You are not expected to directly benefit from this research, however, as a result of this work we will advance our knowledge regarding the effects of mild head impacts. The proposed study is to identify diagnostic tools for more severe traumatic brain injury such as concussion. This work is one of the first steps to unravel public health concern

in concussion and subconcussion, using safe and state-of-art methodologies.

CONFIDENTIALITY

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Your identity will be held in confidence in reports in which the study may be published and data will be stored in the Indiana University online server, and data collection sheets will be stored in a locked file cabinet in a locked room.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the Indiana University Institutional Review Board or its designees, and (as allowed by law) state or federal agencies, specifically the Office for Human Research Protections (OHRP) who may need to access your research records.

COSTS

Taking part in this study may lead to added costs to you or your insurance company. If you experience concussion-related symptoms, you or your insurance company will be responsible for the following costs: doctor's office visit, medications, and neuroimaging. You will not be responsible for any of study-specific costs.

PAYMENT

You (will) receive payment for taking part in this study. You will be reimbursed at an hourly rate set to $10. Because this study period is 6 hours total in a 2-day span, you will receive reimbursement at the end of completion ($60). If you terminate the study participation during the study duration, you will be reimbursed hourly up to the termination point.

COMPENSATION FOR INJURY

In the event of physical injury resulting from your participation in this research, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled. If you are participating in research that is not conducted at a medical facility, you will be responsible for seeking medical care and for the expenses associated with any care received.

CONTACTS FOR QUESTIONS OR PROBLEMS

For questions about the study or a research-related injury, contact the researcher, Keisuke Kawata, PhD at 812-855-5244. If you cannot reach the researcher during regular business hours (i.e., 8 a.m. to 5 p.m.), please call the IU Human Subjects Office at 812-856-4242 or 800-696-2949. After business hours, please call Keisuke Kawata, PhD at 870-210-9918.

In the event of an emergency, you may contact Keisuke Kawata, PhD, at 870-210-9918.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or offer input, contact the IU Human Subjects Office at 812-856-4242 or 800-696-2949.

VOLUNTARY NATURE OF THIS STUDY

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. Your decision whether or not to participate in this study will not affect your current or future relations with Indiana University.

Your participation may be terminated by the investigator without regard to your consent in the following circumstances: you elicit visible disorientation due to the heading protocol or any of measurements. It is to ensure safety for you and research environment.

SUBJECT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study.

I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Subject's Printed Name:_____

Subject's Signature:_____ **Date**:_____
(must be dated by the subject)

Printed Name of Person Obtaining Consent:

Signature of Person Obtaining Consent:_____ **Date**:_____