University of Nebraska Medical Center
NEBRASKA'S HEALTH SCIENCE CENTER

Office of Regulatory Affairs (ORA)
Institutional Review Board (IRB)

April 11, 2024

Madhur Mangalam, PHD
Biomechanics
UNO - VIA COURIER

IRB # 0055-23-EP

TITLE OF PROPOSAL: Network analysis of bodywide coordination supporting suprapostural dexterity

DATE OF CHANGE REQUEST *04/03/24*

DATE OF IRB EXPEDITED REVIEW: *04/11/24*

DATE OF IRB APPROVAL: *04/11/24*

The UNMC IRB has completed its review of the above mentioned Request.

This letter constitutes official notification of approval of the following:

- IRB Application Version 4
- Consent Form Version 3

The IRB has determined that the amended research protocol continues to satisfy all the criteria set forth at 1) 45 CFR 46.111; and 2) HRPP policies. The IRB has not required re-consent of currently enrolled subjects.

All copies of the outdated consent form must be discarded immediately. The previously approved IRB stamped form was automatically archived by the RSS electronic system and can be found under the heading ARCHIVED CONSENTS.

You are authorized to implement all changes accordingly.

Respectfully Submitted on Behalf of the IRB,

Signed on: 2024-04-11 17:27:38.493

Sue Logsdon, MS, CIP
IRB/SROC Analyst III
Office of Regulatory Affairs

Biomedical
SECTION I

Therapeutic/Non-Therapeutic
Does your research involve a drug, medical device, technique or other intervention or strategy (including means like diet, cognitive therapy, behavioral therapy, exercise) to diagnose, treat or prevent a particular condition or disease: "THERAPEUTIC RESEARCH"?
No

1. Title of Protocol:
Network analysis of bodywide coordination supporting suprapostural dexterity

Is a OneChart/EPIC Subject Friendly Short Title needed?
No

2. Responsible Personnel:
A. Principal Investigator (PI):
Mangalam, Madhur - Department of Biomechanics - 706-804-1678 - mmangalam@unomaha.edu - alt #: 402-554-3225 - degree: PHD

B. Secondary Investigator (SI):
Barfi, Mahsa - Biomechanics - 402-830-2776 - mbarfi@unomaha.edu - alt #: 402-554-3225 - degree: MS

Deligiannis, Theodoros - - - - alt #: 402-554-3225 - degree: MS

Schlattmann, Brian Alan - Biomechanics - 402-304-4087 - bschlattmann@unomaha.edu - alt #: 402-554-3225 - degree: DPT

C. Participating Personnel:
Kingston, David - Biomechanics - 531-225-7718 - dkingston@unomaha.edu - alt #: 531-225-7718 - degree: PhD

Magalhaes, Fabricio - - - fmagalhaes@unomaha.edu - alt #: 402-554-6340 - degree: PhD

Yamaguchi, Felipe - fyamaguchi@unomaha.edu - alt #: 402-554-6383 - degree: PhD

D. Lead Coordinator:

E. Coordinator(s):

Are you adding a clinical trial management group?
No

F. Data/Administrative Personnel:

G. Are you a student or house officer?
No

3. Funding Source:
Check all that apply and provide the source of the funding.
Cooperative Group:
Center for Clinical and Translational Research (CCTR)
Federal (e.g., NIH) Grant - Provide source:
Other Grant:
♦ Departmental funding
Commercial - Provide company name:
Department of Defense
Other - Provide source (e.g. personal funding):

4. Deadline for IRB Approval:
♦ Yes - Explain and provide date: 15 February, 2023; the IRB needs to be approved urgently for COBRE Phase II award funding
No

5. Contract:
Is there a contract associated with this study?
No

6. Agreements
Is there a Material Transfer Agreement (MTA) associated with this study?
No

Is there a Data Use Agreement (DUA) associated with this study?
No

Is there a Data Transfer Agreement (DTA) associated with this study?
No

7. Study Sites:
A. Provide the names and locations of all study sites where this research will be conducted under the oversight of the UNMC IRB or Joint Pediatric IRB.
Biomechanics Research Building, UNO

B. Will the research be conducted at external sites under the oversight of an external IRB?
No

C. Does UNMC, TNMC, CHMC or UNO serve as the lead site with responsibility for data and/or safety monitoring?
Yes

List the sites.
Biomechanics Research Building, UNO

D. Does this study involve any international sites where the PI will either; 1) conduct 2) supervise or 3) receive / ship HBM or data to / from UNMC?
No

E. Does this study involve face to face contact with subjects?
Yes

8. Principal Investigator Assurance
The PI understands and accepts the following obligations to protect the rights and welfare of research subjects in this study:

- **All information in this application is complete and accurate.**
- **I will conduct the research as described in the application and the protocol.**
- **I will not initiate any change without IRB approval except when it is necessary to reduce or eliminate a risk to the subject.**
- **I will ensure that all research personnel are qualified and properly trained.**
- **I will fulfill my responsibilities as PI, described in**

https://guides.unmc.edu/books/hrpp-policies-and-procedures/page/126-pi-qualifications-and-responsibilities

- **I will follow all applicable HRPP and institutional polices, and all applicable laws, statutes and regulations.**

Mangalam, Madhur - 2024-04-03 16:51:00.810

9. Principal Investigator Financial Interest Disclosure

A. As the PI, I declare:

♦ I have no financial interest in this research.

I have a financial interest in this research.

B. As the PI, I understand

♦ I must disclose any change in my financial interest during the course of this research within five (5) business days from the time the change becomes known.

C. As the PI, I certify that:

♦ No Responsible Personnel have a financial interest in this research.

The Responsible Personnel listed below have informed me that they have a financial interest in this research.

D. I have informed all Responsible Personnel that if there is any change in their financial interests during the course of this study it must be disclosed within five (5) business days from the time the change becomes known.

Mangalam, Madhur - 2024-04-03 16:51:00.810

SECTION II

PROTOCOL ABSTRACT

1. Provide a brief (less than 2500 characters) abstract of the research protocol. (2500 characters)
This summary should include: 1)) a brief description of the purpose of the study, 2) eligibility criteria, 3) interventions and evaluations and 4) follow-up.

Prevailing understandings of movement disorders characterize broken movements in a piecewise fashion, for instance, focusing on motor control, muscle tone, posture, or cognition independently of each other. These fractured approaches to movement coordination are blind to the body's functional integrity. However, dexterity is global, functional coordination spanning the whole body. In other words, task completion draws on fundamental interactivity allowing the body to coordinate various anatomical parts. Understanding this interactivity is thus paramount to developing novel rehabilitative interventions to prevent falls and improve the quality of life in pathological populations. This project integrates a customizable life-size Trail Making Test with posturography, whole-body movement tracking, and eye tracking, along with state-of-the-art cascade modeling and network analysis methods to assess functional coordination across the whole body. We will leverage causal network analyses of multiplicative interactions instrumental in previous studies of whole-body exploratory motor behavior but not yet utilized in studying suprapostural dexterity. Aim 1 will investigate how multiplicative interactions among movement-system components support suprapostural dexterity. We hypothesize that maintaining an upright stance would produce a functional network of multiplicative interactions among movement-system components. We also hypothesize that participating in the Trail Making Test would produce a succession of distinct, modular networks of multiplicative interactions among movement-system components. Aims 2 will investigate how multiplicative interactions among movement-system components support suprapostural dexterity in the face of postural instability. We hypothesize that destabilizing contact with the ground surface when maintaining an upright stance will produce modular networks of multiplicative interactions with increased connectivity among these modules compared to stable standing. We also hypothesize that destabilizing contact with the ground surface in the Trail Making Test would produce a succession of distinct, modular networks of multiplicative interactions with increased connectivity among these modules compared to stable standing. This modeling framework offers a new way to understand suprapostural dexterity and its breakdown in various movement disorders in light of recent theoretical developments in cascade modeling and network physiology.

PURPOSE OF THE STUDY AND BACKGROUND

2. Purpose of the Study

What are the specific scientific objectives of the research?
This project aims to investigate how multiplicative interactions among movement-system components support suprapostural dexterity. The project integrates a customizable Trail Making Test (TMT) with posturography, whole-body movement tracking, and eye tracking, along with state-of-the-art cascade modeling and network analysis methods to assess functional coordination across the whole body. The project has two specific aims: (1) to investigate how multiplicative interactions among movement-system components support suprapostural dexterity, and (2) to investigate how multiplicative interactions among movement-system components support suprapostural dexterity in the face of postural instability. The project hypothesizes that maintaining an upright stance and participating in the Trail Making Test would produce modular networks of multiplicative interactions among movement-system components, and that destabilizing contact with the ground surface would produce modular networks of multiplicative interactions with increased connectivity among these modules compared to stable standing.

3. Background and Rationale
Describe the background of the study. Include a critical evaluation of existing knowledge, and specifically identify the information gaps that the project is intended to fill.
Dexterity is global, functional coordination spanning the whole body (Bernstein, 1967; Chiel and Beer, 1997; Profeta and Turvey, 2018; Turvey, 2007, 1990; Turvey and Fonseca, 2014), but movement science risks taking a fractured approach to investigate how dexterity is supported. Diagnoses of movement disorders are on the rise in the United States, the most common being due to stroke (Tsao et al., 2022; Yousufuddin and Young, 2019) and Parkinsons disease (Jankovic, 2009; Steeves et al., 2012). Prevailing understandings of these disorders characterize broken movements in a piecewise fashion, for instance, focusing on motor control, muscle tone, posture, or cognition independently of each other. Likewise, rehabilitative interventions target the limb or body parts most affected by the disorder seeking to support the whole body by mending the broken part. However, this perspective can be blind to the body's functional integrity. Functionality can override anatomical separability, which is rarely more evident than in suprapostural dexterity when the body must complete a task while maintaining an upright stance. On the prospective path towards a goal, whatever begins at one or more anatomical locations can quickly spread through the whole body, destabilizing the body on the way to task completion. Indeed, the compromised coordination between task engagement and postural instability accentuates the risk of falling in pathological populations (Barr et al., 2017; Canning et al., 2014; Ekbom and Ulfberg, 2009; Fasano et al., 2017; Rascol et al., 2015). In other words, task completion draws on fundamental interactivity allowing the body to coordinate various anatomical parts. This coordination may be more vital to healthy movement than individual anatomical parts. Understanding this interactivity is thus paramount to developing novel rehabilitative

interventions to prevent falls and improve the quality of life in pathological populations.

This project investigates how multiplicative interactions support suprapostural dexterity from two complementary premises. First, movement science has established that postural stability requires a modular structure of functional networks shaped by the anatomical constraints of the musculoskeletal system (Boonstra et al., 2019, 2016, 2015; Esteve-Altava et al., 2015; Kerkman et al., 2020, 2018; Murphy et al., 2018). This arrangement indicates a soft assembly and disassembly of functional modules as an individual engages in a task and responds to changing task demands, respectively. Second, movement science has yet to grapple with the multiplicative interactions among movement-system components producing highly complex and unpredictable behaviors beyond the scope of dominant linear modeling approaches (Kelty-Stephen et al., 2013, 2022; Kelty-Stephen and Mangalam, 2022a; Mangalam and Kelty-Stephen, 2022). Accordingly, the scientific premises for this proposal are that the dominant network approaches to dexterity are linear, and network approaches can give voice to the nonlinearity we all know is there.

The prevailing dogmatic views on dexterity take a fractured approach to investigating how dexterity is supported, often focusing on motor control, muscle tone, posture, or cognition independently of each other. However, dexterity is global, functional coordination spanning the whole body (Bernstein, 1967; Chiel and Beer, 1997; Profeta and Turvey, 2018; Turvey, 2007, 1990; Turvey and Fonseca, 2014). For instance, postural fluctuations produce translations and rotations of visible surfaces specific to the objects spatial relationships in the visual field. These movement-induced translations and rotations compose an optic flow that provides visual support for the subsequent movement. Thus, subtle sway offers the sighted organism a rich source of information about objects layouts in the visual field. The visual layout then presses the postural system into a poise for engaging with objects and events (Mangalam et al., 2021). Hence, functionality overrides anatomical separability when the body must complete a task while maintaining an upright stance.

A series of recent studies have modeled postural stability as a modular structure of functional networks shaped by the anatomical constraints of the musculoskeletal system (Boonstra et al., 2016, 2015; Esteve-Altava et al., 2015; Kerkman et al., 2020, 2018; Murphy et al., 2018). This arrangement indicates a soft assembly and disassembly of functional modules as an individual engages in a task and responds to changing task demands, respectively. However, critically, movement science follows the prevailing tradition in network approaches of preserving spatial or structural information while collapsing across time (Bartsch et al., 2015; Bashan et al., 2012; Gosak et al., 2022; Ivanov et al., 2016; Rizzo et al., 2020). Collapsing variability across time leads to the lack of generalizability of results because variability is not the same across space and time. In contrast, cascades carry information about uncollapsed time, the texture, and the variation that dexterous posture will

have as the body coordinates longer timescale factors like intention for task completion with shorter-timescale factors like perturbations and corrective movements. Cascade modeling allows us to articulate how seemingly differentiated forms can arise from fluid interactions of the movement-system components across many timescales (Kelty-Stephen et al., 2022, 2013; Kelty-Stephen and Mangalam, 2022b). Cascades operate through the loose nesting of finer motoric details within larger motoric degrees of freedom (e.g., motor neurons within bundles of muscle fiber, muscles within joint-centered synergies, and so on) that allow dexterous behavior to adapt flexibly to constraints changing on the way to task completion. We have previously shown this capacity for cascades to knit events across many timescales is similar in postural sway, no matter whether we load the upper body (Furmanek et al., 2020; Kelty-Stephen et al., 2020), destabilize contact with the ground surface (Kelty-Stephen, 2018; Mangalam and Kelty-Stephen, 2021), or increase visual effort (Mangalam et al., 2021). However, treatment could be tailored and targeted if we know what specific network structures support suprapostural dexterity and how these networks assemble and dissemble.

A significant challenge of standard linear network models has been the discontinuity between one functional module and the next. The precision of cascade-driven network modeling will allow us to understand suprapostural dexterity without switching between different control modes. Cascade modeling allows us to articulate how seemingly differentiated forms can arise from similar fluid interactions across many timescales (Kelty-Stephen et al., 2022, 2013; Kelty-Stephen and Mangalam, 2022b). This capacity for cascades to extend across timescales appears similarly in postural sway, no matter whether we load the upper body (Furmanek et al., 2020; Kelty-Stephen et al., 2020), destabilize contact with the ground surface (Kelty-Stephen, 2018; Mangalam and Kelty-Stephen, 2021), or increase visual effort (Mangalam et al., 2021). Indeed, network modeling of cascade-like interactivity may reflect control parameters governing bodily coordination across the timescales of the fastest reflex to the slowest movement unfolding across the entire task. This modeling framework offers a new way to understand suprapostural dexterity in light of recent theoretical developments in cascade modeling and network physiology.

We will use network modeling of cascade-like interactivity as a fresh way to understand suprapostural dexterity in light of recent theoretical developments in cascade modeling and network physiology. The precision of cascade-driven network modeling will allow us to understand suprapostural dexterity without implying any discontinuity between one functional module and the next. Healthy adults will maintain an upright stance on a stable surface in one condition and perform the Trail Making Test while maintaining an upright stance in the other. We hypothesize that maintaining an upright stance would produce a functional network of multiplicative interactions among movement-system components (Hypothesis 1.1). The Trail Making Task has been shown to measure several capabilities

such as cognitive flexibility, alternating attention, sequencing, visual search, and motor speed, among other functions (Bowie and Harvey, 2006; Reitan, 1958; Sanchez-Cubillo et al., 2009). Performing the Train Making Task must introduce longer-timescale constraints on the postural system already satisfying the shorter-timescale demands of postural stability. It is expected that the culmination of shorter-timescale postural constraints and longer-timescale constraints imposed by the Trail Making Task will produce more differentiated network configurations or modular networks. Accordingly, we hypothesize that taking part in the Trail Making Test would produce a succession of distinct, modular networks of multiplicative interactions among movement-system components (Hypothesis 1.2).

Aim 1 approach network modeling from the vantage point of traditional modeling that these modular networks should be static. In Aim 2, we will relax this premise to investigate how the cascade-like interactivity exhibits a continuum of variability within so-called modular networks and could underwrite the transitions between separate network configurations. Specifically, we will investigate how shorter-timescale perturbations destabilizing the upright stance interact with the longer-timescale constraints on task completion to facilitate transitions among different network configurations. We base our predictions on recent findings of functional brain networks, which suggest that performing two tasks simultaneously or in close succession relies on the flexible reconfiguration of the brain networks (Alavash et al., 2015; Ekman et al., 2012; Hilgetag et al., 2001; Lam and Shin, 1998). Indeed, performance in different concurrent tasks benefits from unique functional brain networks at various timescales: integration of local, intermediate, or global networks (Alavash et al., 2015). Furthermore, the inability of the brain networks to sustain two separate topological configurations at once, each supporting the performance in one of the dual-task components, causes moment-to-moment fluctuations in the dual-task behavior (Alavash et al., 2016). Accordingly, we will examine the extent of modularity and the strength of connectivity between modular networks on multiplicative interactions as part of Aim 2.

Aim 2 is about unseating one of these modular networks with a perturbation and showing that the reorganization of these networks can be understood from the cascade-like interactivity across the body. Healthy adults will maintain an upright stance on an unstable surfacea balance boardin one condition and perform the Trail Making Test while maintaining an upright stance on the same unstable surface in the other. We hypothesize that destabilizing contact with the ground surface when maintaining an upright stance will produce modular networks of multiplicative interactions with increased connectivity among these modules compared to stable standing (Hypothesis 2.1). We hypothesize that destabilizing contact with the ground surface when taking part in the Trail Making Test would produce a succession of distinct, modular networks of multiplicative interactions with increased connectivity among these modules compared to stable standing (Hypothesis 2.2).

Since fewer modular networks typically exhibit sparser intra-modular and denser inter-modular connections, we expect an inverse correlation between modularity and between-module connectivity from a theoretical standpoint.

CHARACTERISTICS OF THE SUBJECT POPULATION

4. Accrual
A. Is this study conducted solely at sites under the oversight of the UNMC IRB (e.g. UNMC, Nebraska Medicine, CHMC, UNO)?
Yes

1. How many subjects will need to be consented (per group, as applicable) in order to achieve the scientific objectives of the research?
50 healthy adults; 25 men and 25 women

2. What is the statistical or other justification for the total number of subjects described above?
Sample size determination was made based on previously observed values of statistical descriptors of movement variability in older and younger adults (older: H = 0.64±0.08; younger: 0.76±0.07 (Hunt et al., 2014; Kaipust et al., 2013; Raffalt et al., 2021; Vaz et al., 2019; Vaz et al., 2020) and the procedure outlined in Kuznetsov and Rhea (2017). The method entails generating simulated datasets with known parameters. Power Analysis conducted across 1000 simulated datasets revealed that 16 participants per group will yield 86%, 94%, and 100% power to detect a difference of 0.1, 0.05, and 0.3 in H for fixed effects of Sex and the two nestings of experimental manipulation. We will recruit N = 25 participants per age group to account for possible attrition, equipment failures, etc.

3. How long do you estimate it will take to accrue the required number of subjects?
We will take about 60 weeks = 15 months at the rate on one participant per week, including 10 week for vacations etc.

5. Gender of the Subjects
A. Are there any enrollment restrictions based on gender?
No

6. Age Range of Subjects
A. Will adults be enrolled ?
Yes

1. What is the age range of the adult subjects?

19 to 35 years old healthy young adults will participate (a separate study will be planned to include middle age and older adults). Since the proposed project has a within-subjects design, each participant will be subjected to each experimental condition.

2. What is the rationale for selecting this age range?
Our choice of 19 to 35 years old participants is based on two reasons: (i) the movement system starts to show slowing and deterioration in most adults as they reach 40 years of age; and (ii) we plan a future study with comparisons to middle-aged and older adults to study how the movement system deteriorates with age.

B. Will children (18 years of age or younger) be included in this research?
No

1. What is the justification for excluding children from participating in this research?
♦ Research is irrelevant to children (e.g. disease or condition rarely encountered in children).
Knowledge being sought in the research is already available for children or will be obtained from another ongoing study.
A separate study in children is warranted and preferable.
Insufficient data are available in adults to judge the potential risk in children.
Other. Explain.

7. Race and Ethnicity
Are there any subject enrollment restrictions based upon race or ethnic origin?
No

8. Vulnerable Subjects
A. Will prisoners be included in the research?
No

B. Select from the list all of the vulnerable populations that will specifically be recruited to participate in this research.
Decisionally-impaired persons
Critically ill patients
Students of the investigator
Employees of the investigator
Educationally disadvantaged individuals
Socially or economically disadvantaged individuals
Individuals with a stigmatizing illness or condition

Individuals from a marginalized social or ethnic group
Other.
♦ No vulnerable subjects will be specifically recruited

9. Inclusion Criteria
What are the specific inclusion criteria?
Participants must (i) be able to provide informed consent, (ii) be able to stand and walk independently without an assistive device, (iii) not self-report diagnosis of a neurological disease, and (iv) not a self-report diagnosis of any limb disabilities, injuries, or disease.

10. Exclusion Criteria
What are the specific exclusion criteria?
N/A

11. Pregnancy and Contraception Requirements
A. Are women of child bearing potential (WOCBP) included in this research?
Yes

a. Are there any specific contraception requirements for subjects?
No

1. Provide justification for absence of contraception requirements
♦ There are no interventions that are likely to be of risk to a fetus
Investigational drug(s) is (are) not systemically absorbed
Investigational drug(s) is (are) systemically absorbed, but there is no evidence from human studies, or from clinical experience, that there is risk to a fetus
Other

B. Are pregnant women included in this research?
No

1. Provide justification for excluding pregnant women
Investigational drug(s) is (are) absorbed systemically, and there is evidence from animal or human studies, or from clinical experience, that there is risk to a fetus **OR** investigational drug(s) is (are) absorbed systemically, and there is a well-understood mechanism of action that may result in risk to a fetus
Intervention includes a procedure expected to be of risk to a fetus (eg, exposure to ionizing radiation, maximal exercise test)
Research is not relevant to pregnant women (e.g. disease or condition rarely encountered in

pregnant women)
Knowledge being sought in the research is already available for pregnant women or will be obtained from another ongoing study
A separate study in pregnant women is warranted and preferable
♦ Physiology of pregnancy precludes generalization to other populations
Other - explain

2. Describe how pregnancy status will be assessed (eg, self-report, urine pregnancy test, blood pregnancy test) and the frequency of monitoring during participation in the research.
Self-report

3. Describe the plan should a female subject, or the partner of a male subject, become pregnant while research interventions are on-going (or during the period that contraception is required following the completion of the intervention).
Subjects will be recruited for one data collection session lasting no more than 3 hours. Therefore, contraception or pregnancy status will unlikely change during the described protocols.

C. Are breast feeding women excluded in this research?
No

Provide justification for the inclusion or exclusion of breast feeding women.
There is no added danger to breast feeding women during sighted or blindfolded walking sessions in this protocol.

METHODS AND PROCEDURES (NON-THERAPEUTIC)

12. Methods and Procedures Applied to Human Subjects
A. Describe the research plan, including all procedures, interventions, evaluations and tests. If subjects will be randomized to a specific intervention, the randomization plan should be explained.
Tasks, procedure, and instructions to the participant
Participants will be tested in an indoor laboratory in the Biomechanics Research Building at the University of Nebraska at Omaha. After taking informed consent, participants will be fitted with retroreflective markers and an eye tracker (see below). In Aim 1, participants will maintain an upright stance on a stable surface a pair of force plates in one condition and perform the Trail Making Test while maintaining an upright stance in the other. The Trail Making Task will be presented on a projector screen and involve drawing a trail through jumbled numbers. In Aim 2, participants will maintain an upright stance on an unstable

surface a balance board placed on the force plates in one condition and perform the Trail Making Test while maintaining an upright stance on the same unstable surface in the other. Each trial is expected to last about seven-eight minutes and will be repeated if the participants lost balance at any time between the trial for a maximum of two repetitions. Participants will be subjected to three trials of each of the four conditions in a single experimental session lasting 120 mins. The order of the 12 trials will be randomized for each participant.

Balance board
Balance boards, which include rocker boards and wobble boards, are a fitness tool people can stand on while performing exercises to help improve balance and posture, aid in rehabilitation, prevent lower body injuries, and increase core strength, among other benefits. We will use a lateral balance board as show in the attached picture.

Posturography
Participants will stand on dual 40×60 cm floor-embedded force plates (400600HPS, AMTI Inc., Watertown, MA) with one foot on each force plate. Participants will be given no additional instructions that can impose artificial constraints on the posture. Ground reaction forces will be recorded at 200 Hz.

Motion tracking
Participants will be outfitted with a form-fitting compression suit, lab-provided athletic shoes in their size, and a full-body, 79-marker retroreflective marker set before the study. Marker trajectories in 3D will be collected at 200 Hz using a 17-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA). An RGB camera will record the laser pointer traces on the projector screen. A wireless receiver will be connected to the motion capture system to track eye movements in synchrony with the kinematic data.

Combining eye tracking and motion capture
Participants will wear an eye tracker (100 Hz, Glasses 2, Tobii, Stockholm, Sweden). Before data collection, participants will look at a calibration matrix projected on the screen with calibration marks at known locations. The pixel coordinates of calibration marks will be used to transform the gaze data into the frame of reference of the kinematic data from pixels to millimeters. At each subsequent frame, gaze data will be translated and rotated according to the motion capture system's 6-DoF measurements of head position. Eye tracking will provide a rich resource for pilot analyses of visual exploration during the suprapostural task. Primarily it would allow us to make better contact between the movement dynamics and existing theories of visual cognition. Secondarily, it would inform subsequent experimental designs; for example, we might experimentally manipulate the distance between visual targets within or beyond the comfortable, self-selected ranges.

B. Are all of the procedures, interventions, evaluations and tests being performed solely for research purposes?
Yes

C. Describe briefly the statistical methods used to analyze the data (or reference the appropriate section of the detailed protocol or grant).
Pre-processing of posturography and motion-tracking data
Center of Pressure (CoP) planar Euclidean displacement (PED) series: The ground reaction forces recorded from the two force plates will be combined to yield a 2D CoP series, describing the CoP position along the participants anterior-posterior and medial-lateral axes. A 1D CoP PED series will be obtained for each 3D CoP series, describing CoP displacement along the body's transverse plane. Center of Mass (CoM) spatial Euclidean displacement (SED) series: The bodily CoMs position will be estimated by submitting segment lengths of the head, trunk, pelvis, left and right hand, forearm, upper arm, thigh, shank, and foot to the equations from Zatsiorsky and Seluyanov (Zatsiorsky and Seluyanov, 1985), yielding a 3D series describing CoM position along the participants anterior-posterior, medial-lateral, and superior-inferior axes. A 1D CoM SED series will be obtained for each CoM series, describing CoM displacement in 3D. Marker SED series: Motion tracking of each reflective marker will yield a 3D series describing its position along the participants medial-lateral, anterior-posterior, and superior-inferior axes. A one-dimensional SED series will be obtained for each marker, describing the displacement of that marker in 3D.

Mapping gaze to the TMT stimulus
The L and R eyes' gaze data will be independently recorded, and for analytical purposes, we will compute the average gaze location between the two eyes for each time point. The transformation of all gaze data will make it relative to the screen. The X and Y coordinates of the gaze position, the timestamp, and the matching world-camera video frame number will be included for each sample in the eye-tracking data file (normalized w.r.t. the world-camera frame dimensions).

Assessing multifractality due to nonlinearity
Multifractality refers to blending processes across different timescales, producing emergent structures. Multifractal spectrum width will be estimated using Chhabra and Jensens (1989) direct method. A non-zero width will indicate interactions in component processes producing rapidly changing periods of variability, such as small and large changes in fluctuations. To identify whether a nonzero width reflects multifractality due to nonlinearity, the multifractal spectral width for the original series will be compared to those for 32 Iterated Amplitude Adjusted Fourier Transform (IAAFT) surrogates (Ihlen, 2012; Schreiber and Schmitz, 1996). IAAFT randomizes original values time-symmetrically around the autoregressive structure, generating surrogates that randomize phase ordering of the original series spectral

amplitudes while preserving linear temporal correlations. The one-sample t-statistic takes the subtractive difference between the multifractal spectrum widths for the original series and 32 surrogates, dividing by the standard error of the spectrum width for the 32 surrogates. The greater the value of the t-statistic, the greater the multifractality in the original series due to nonlinear as opposed to linear sources.

Network modeling of multiplicative interactions
Vector autoregression (VAR) analysis will be used to model multiplicative interactions across the CoP, CoM, and 79 markers, represented in the model as (CoP, CoM, M1, M2, ,,,, M79). VAR captures interdependencies amongst concurrent series and will model the effects of t-statistic across anatomical locations in subsequent segments. VAR will yield a temporal trajectory of weights for each combination, defining a directional weighted musculoskeletal network for each participant and task condition. These functional networks will be transformed into binary networks to compare with the anatomical network. Thresholding the weightsusing a single, unique threshold value corresponding to the percolation threshold (Esfahlani and Sayama, 2018)will yield a minimally connected network across task conditions. In this sparse network, each node will be connected to at least one node by an edge at one of the layers of the multiplex network.

Statistical analysis
A full-factorial regression model will test the impulses and responses of each marker position. Impulse and Response will serve as class variables indicating the locations of impulse and response variables. Statistical significance will be interpreted as evidence of the flow of nonlinearities in movement fluctuations between the corresponding pair of anatomical locations, with the flow direction from the Impulse variable to the Response variable. Statistical significance will be set at a Type I error rate of 5%.

Extraction of functional musculoskeletal modules
The Louvain algorithm will extract functional musculoskeletal modules from the entire network. Consensus clustering will be implemented to achieve a stable partition(Lancichinetti and Fortunato, 2012). Multiplex modularity analysis will identify the functional musculoskeletal modules across different task conditions---MolTi software (https://github.com/gilles-didier/MolTi) will be utilized to identify functional musculoskeletal modules within multiplex networks by optimizing multiplex modularity through the modified Louvain algorithm.

Comparison of functional musculoskeletal networks across task conditions
The networks will be coarse-grained to compare functional musculoskeletal networks across task conditions (Kujala et al., 2016). The functional modules estimated across task conditions will coarse-grain the binary networks and then compare the strength of the inter-

and intra-module connections across task conditions. The nodes in clustered networks represent modules, and the edges signify the relationships between modules.

D. Does this study involve the collection of blood, urine, saliva or other human biological material (HBM)?
No

DRUGS, BIOLOGIC DRUGS AND DEVICES

13. Drugs and Biologic Drugs
1. Does this research involve the use of drugs or biologics?
No

14. Devices
1. Does this research involve a medical device(s) (including an in vitro device [IVD] (assay), and medical software)?
No

CONFIDENTIALITY AND PRIVACY

15. Confidentiality and Privacy
A. Describe where research data will be stored. Check all that apply.
Box@unmc.edu (secure UNMC or UNO designated cloud-based storage site)
♦ Microsoft Office 365 application (including SharePoint, OneDrive for Business, Teams or Streams) (UNMC, UNO or NU system instance) (secure UNMC or UNO designated cloud-based storage site)
Other secure UNMC or UNO designated cloud-based storage site - describe:
OnCor Clinical Trial Management System (secure server at UNMC, CHMC, Nebraska Medicine, and/or UNO)
CCORDA database (biostatistics) (secure server at UNMC, CHMC, Nebraska Medicine, and/or UNO)
RITO-hosted databases (for example, REDCap, CV-QOR, Onchem Trials, XNAT) (secure server at UNMC, CHMC, Nebraska Medicine, and/or UNO)
Nebraska Medicine PACS (for image files) (secure server at UNMC, CHMC, Nebraska Medicine, and/or UNO)
Other secure server at UNMC, CHMC, Nebraska Medicine, and/or UNO - describe:
On an NSRI or designated high security .gov storage site
On a VA-approved storage vehicle for a VA-approved study
On a remote secure server and/or database maintained by the sponsor accessible through the internet

On a secure server and/or database hosted and maintained by another institution accessible through the internet
On a device or mobile application provided by the sponsor to upload data to a coordinating center or central database
On a device or mobile application being developed by a sponsor or by a UNMC, CHMC or UNO investigator
On a device or mobile application that connects to the internet through UNMC or NM network (wired or wireless)
♦ On an encrypted, password protected portable computer, or flash drive
Other - describe:
In hard copy (other than signed Consent Forms)

B. Will any of the following subject identifiers be recorded (at any time) in association with the research data?
No

1) Indicate the subject identifiers that will be recorded. Check all that apply.
♦ Name
♦ DATES (e.g. date of study visit, date of sample collection, birth, admission, discharge)
Postal address information: street address, city, county, precinct, ZIP code
♦ Telephone numbers
Fax numbers
♦ Electronic mail addresses
♦ Social Security numbers
Medical Record numbers
Health plan beneficiary numbers
Account numbers
Certificate/license numbers
Vehicle identifiers and serial numbers, including license plate numbers
Device identifiers and serial numbers
Web Universal Resource Locators (URLs) Internet Protocol (IP) address numbers
Biometric identifiers, including finger and voice print
Full face photographic images [and any comparable images]
No Identifier

2) Will a unique subject identifying number (e.g., S1, S2, S3), characteristic or code be used to link data to any of the identifiers listed above?
Yes

a. Where will the key (that links the unique subject identification code to the subject's name or other identifier) be stored?
UNO designated Microsoft Office 365 application (including SharePoint, OneDrive for Business, Teams or Streams)

b. Does the code number include the subject's initials or other subject identifier as part of the code?
No

3) What is the justification for recording the specific subject identifiers listed above? Check all that apply.
♦ Schedule appointments
Collect continuous clinical information from the medical records
Follow-up with subjects
Link stored tissue with subject identification for it to be withdrawn in the future if requested
♦ Compensation
Other. Explain.

4) How long will the subject identifiers be maintained in association with the research data?
The data will be maintained for at least seven years following the completion of the study.

5) How will all of the identifiable research data be destroyed (e.g., all identifiers stripped from the data and destroyed, hard copies shredded etc) when the identifiable data is no longer required?
Upon the completion of all data collections, all copies of the key will be deleted from the server, hard copies will be shredded, and all identifiers will be deleted from electronically stored data.

C. Will research data that contain subject identifiers be disclosed to:
Other investigators at UNMC, NM, UNO or CHMC who are not listed in Section I of this application?
No

2. Investigators outside of UNMC, NM, UNO or CHMC?
No

3. Will research data that contain subject identifiers be disclosed to any commercial sponsor or contract research organization (CRO), or to any other external organization

or entity (e.g., NCI cooperative groups)?
No

D. What provisions will be in place to protect the subject's privacy? Check all that apply.
♦ Ensuring that only personnel listed on the IRB application Section I.3(A-E) are present during the consent process.
♦ Ensuring that the fewest number of individuals possible are aware of the subject's participation in the research.
♦ Ensuring that the research activities are performed in as private of a place as possible.
Other. Explain.

E. Does this research involve data banking at UNMC, NM, UNO or CHMC, or by an outside organization (e.g. NCI Cooperative Group, pharmaceutical company) for future research that is not related to this study?
No

RISK/BENEFIT ASSESSMENT

16. Potential Risks
What are the potential risks associated with each research procedure, intervention, evaluation and/or test? If data are available, estimate the probability that a given harm may occur and its potential reversibility.
The potential risks of standing are similar to general bouts of light physical activity, the most likely one being fatigue due to extended standing. The trials in which participants will be asked to maintain balance on a balance board run the risk of losing balance. Balancing on the balance board might pose additional risk of loosing balance and falling. We will cover all surface adjacent to the participant with thick styrofoam to prevent injury in the unlikely case of fall.

17. Risk Classification
What is the overall risk classification of the research?
♦ Minimal risk
Greater than minimal risk

18. Minimization of Risk
A. Describe how the subjects of the research will be monitored by the investigators and other research personnel to ensure their safety.
We will cover all surfaces adjacent to the participant with thick styrofoam to prevent injury in

the unlikely case of a fall when balancing on the balance board. Also, the study will be terminated if the participant report to have any kind of loss of balance while participating in the study.

B. Describe how the data collected will be monitored to ensure the safety of subjects. Identify who will perform the ongoing data and safety analysis, and describe the frequency of data analysis. If there is an independent Data and Safety Monitoring Board (DSMB) provide the charter, or describe (1) the composition of the DSMB membership, (2) the frequency of DSMB meetings and reports.
Collected data will be temporarily stored on an encrypted, password-protected local hard drive after data collection sessions have been completed. After being uploaded to a secure UNO Office365 server that only the listed personnel will have access to, they will be removed from the local hard drive. Hard paper copies will be stored in a lockable file cabinet within a locked room only accessible to the listed personnel. The PI will perform ongoing data and safety analysis. Data monitoring by the PI will occur every month.

C. Describe the auditing plan for research conducted. Identify who will conduct the audits and specify the audit frequency.
The primary investigator will be in charge of auditing the research (every 2 months) if discrepancies are found between the data collection, analysis, or logging procedures.

D. Describe the specific subject withdrawal criteria.
Participants will be asked throughout the data collection period if they are experiencing any physical discomfort and will be withdrawn from the study if stated that they do experience any physical discomfort. If the subject appears to be off balance or unsteady, they will be withdrawn from the study. Participants only need to express this to an investigator if they desire to withdraw. Suppose any aspect of the research negatively impacts their health or they no longer fit the eligibility criteria at any point in the research. In that case, the participant will be taken off the study. The study does not have any treatment or intervention beyond minimal physical activity. Therefore there is no consequence to the participant for withdrawing from the protocol

E. Describe the stopping rules for the research (e.g., the specific criteria for halting or early termination of the study).
The data collection sessions will be halted for reasons including, but not limited to: injury of any kind during data collection, equipment malfunction that may put the participants in increased harm, signs of physical injury, or expression of physical discomfort. We do not expect participants falling to be common during this project. However, if any participants fall, the study session will be terminated.

F. Describe plans and resources available to promptly address any subject injury.
The Biomechanics Research Building and the Health & Kinesiology Building have Emergency Action Plans that all investigators are familiar with. The procedures are listed in the attached document.

19. Potential Benefits to the Subject
Is there the prospect for direct benefit (eg, research on diagnosis or treatment of disease)?
No

20. Potential Benefits to Society
Describe the potential benefits to society that may reasonably be expected to result from this research.
The knowledge generated by this project will lay the foundations of a new way to understand suprapostural dexterity and its breakdown in various movement disorders.

FINANCIAL OBLIGATIONS AND COMPENSATION

22. Financial Obligations of the Subject
A. Who will pay for research procedures, interventions, evaluations and tests? Check all that apply.
Sponsor
Grant
CRC, CCTR
Costs or fees waived by Nebraska Medicine, UNMC- P, CHMC or CSP
♦ Department/Section funds
Other. Explain

B. Will any of the research procedures, interventions, evaluations and tests described above be charged to the Subject, the Subject's health insurance, or Medicare/Medicaid?
No

C. Are there any other financial obligations that the subject will incur as a result of participating in the study?
No

23. Compensation to the Subject for Participation
A. Will the subject receive any compensation for participation?

Yes

1. Describe the form of compensation, dollar amount (if applicable) and the prorated compensation plan (if applicable).
Participants will be compensated hourly at $10 per hour for participation. Compensation will be prorated for the next full hour. For example, if the experiment lasted two hours and fifteen minutes, participants will be compensated for three hours. Participants will be compensated even if the study session is terminated prior to completion. Prorated compensation will be made regardless of whether withdrawal was voluntary (the participant decides to withdraw from the study) or involuntary (based on withdrawal criteria of the research protocol.)

At the end of the study session, using a laboratory computer, the participant will fill out and sign an online form with their payment details such as name, address, SSN, and citizenship status. None of these things will be recorded by the researcher. The form will then be sent to
the researcher to enter the amount the participant is to be paid and the cost center number for the grant the payment is to come from and submit for departmental approval. Once this is complete it will be sent to the accounting department of UNO for processing. A check will be sent to the participant at the address written on the form.

PRIOR REVIEW

24. Prior IRB Review
A. Has this study (or one substantially similar) been previously submitted to the UNMC IRB (or the Joint Pediatric IRB) and then withdrawn by the investigator for any reason?
No

B. To the best of your knowledge, has this study (or one substantially similar) been considered by another IRB and disapproved?
No

SUBJECT IDENTIFICATION & RECRUITMENT

25. Method of Subject Identification and Recruitment
A. Will prospective subjects learn about the research and then contact the investigator about participation (for example, in response to a print, electronic, radio or television advertisement; referral by a clinician or other specifically for this research)?
Yes

1. If so please describe how prospective subjects will become aware of the research

(for example, by a print, electronic, radio or television advertisement, or thru another mechanism)?
Healthy young adults will be identified and recruited by word of mouth and campus-wide email. Email lists provided by faculty or staff from departments within the University of Nebraska at Omaha will be used for the recruitment email.

2. Who will be responsible for receiving these inquiries from prospective subjects?
Primary and secondary investigators

3. Will prospective subjects be screened for eligibility prior to informed consent?
No

B. Will the investigator make the initial contact with the potential subject to tell him/her about the research (for example, by contacting existing or past previous patients or research participants; or by contacting prospective subjects thru school records, or thru support groups or other Interest Groups; or thru use of the Hospital Opt-In Database)?
No

C. Will this study be listed in the clinical trial registry at www.clinicaltrials.gov?
No

OBTAINMENT OF INFORMED CONSENT

26. Waiver or Alteration of Informed Consent
A. Is a complete waiver or alteration of consent requested?
No

27. Waiver of Signed Consent
Is a waiver to obtain signed consent requested?
No

29. Process of Informed Consent
A. When will the prospective subject/parent(s)/guardian(s)/LAR be approached relative to their/the subject's actual participation in the study?
Potential participants will be scheduled at their earliest convenience.

B. Where will informed consent be obtained, and how will the environment be conducive to discussion and thoughtful consideration?

Informed consent will be obtained in the Biomechanics Research Building on the University of Nebraska at Omaha campus. All consent will take place in one of our evaluation rooms, which are private, similar to a doctor's office. The investigator obtaining consent from the participant will explain all procedures verbally to the participant until they fully understand the risks, benefits, and protocol of the study and feel comfortable to begin the data collection.

C. Who will be involved in the process of consent and what are their responsibilities?
The PI, secondary investigators, and participating personnel will be permitted to consent to participants. All investigators will be responsible for clearly explaining the research study, including the benefits and risks of participation. They will minimize the possibility of coercion or undue influence, and no exculpatory language will be used to imply that the participant is waiving their legal rights.

D. Is there any limitation on the amount of time allotted to the process of consent?
No

E. How will the process of consent be structured for subjects who are likely to be more vulnerable to coercion or undue influence?
We are not recruiting potential participants who may be vulnerable to coercion or undue influence. If investigators suspect the participant may be vulnerable, the participant will not be allowed to participate in the research study.

F. Will non-English speaking subjects be enrolled in this research?
No

Provide justification for exclusion of non-English speaking subjects
A translator is not available to assist this project.

G. How will it be determined that the subject/parent(s)/guardian(s)/LAR understood the information presented?
We will assess participant comprehension using the second suggested method: asking the individual to describe the research in sufficient detail, whereby the subject demonstrates an acceptable level of comprehension of all elements of the consent form.

31. Information Purposely Withheld
Will any information be purposely withheld from the subject during the research or after completion of the research?
No

RESOURCES

33. Describe the resources available to safely conduct this study at each study sites specified in Section I.7.
The Biomechanics Research Building and the Health and Kinesiology Building have Emergency Action Plans that all research personnel is familiar with. All storage, equipment, and emergency first aid kits are located within the building and are adequate for human subjects research.

LITERATURE REVIEW

34. References
Provide a full listing of the key references cited in the background (Section II.3). The references should clearly support the stated purpose of the study.
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SECTION III

SUBMISSION DEADLINE

A. Full Board Review:
The IRB meets twice monthly, on the first and third Thursday of the month, with the exception of January and July when the IRB meets only on the third Thursday of the month. No more than 15 applications (e.g., initial review of a new study, re-review of a tabled study) will be reviewed at each meeting. All reviews are performed on a first-come first-served basis. The IRB meeting schedule and deadline dates can be found on the IRB website at www.unmc.edu/irb.

B. Expedited Review
Applications that qualify for expedited review have no submission deadline and can be reviewed independent of the IRB meeting schedule. Call the Office of Regulatory Affairs for assistance in determining if your study meets the requirements for expedited review.

ADDITIONAL REVIEW REQUIREMENTS

Final IRB approval and release of studies is contingent upon approval by the following UNMC committees or departments. Check the appropriate boxes:
UNMC and NM - Pharmacy & Therapeutics (P&T) Committee (Required for studies involving drugs)
Fred & Pamela Buffett Cancer Center Scientific Review Committee (SRC) (Required for studies involving cancer)
Institutional Biosafety Committee (IBC) (Required for studies involving the use of gene transfer and vaccines)
Investigational Device Review Committee (IDRC) Review by the IDRC is required for all protocols involving the use of investigational or marketed devices
Billing Grid (Required for all studies involving billing for hospital/clinic services)
Coverage Analysis (Departments requiring this analysis have been specified by the Organization)
Conflict of Interest (COI) Management Plan (Required for all studies with declared COI by study personnel)
Sponsored Programs Administration (SPA)/UNeHealth grants and contracts
Pathology approval for collection of tissue samples required for this study
Radiation Committee Approval
Other Review
♦ **None of the above organizational requirements apply to this study**

SECTION IV

COVID-19

Human Subjects Research Safety Plan
For studies involving face-to-face encounters, the research team under the responsibility of the principal investigator will agree to comply with the following safety measures:

1. **Masking of the researcher(s) during a face-to-face encounter**
2. **Cleansing of any surface and/or equipment utilized before and after a subject encounter**
3. **The Biosafety Officer (jenna.mckenzie@unmc.edu) will be notified if obtaining saliva, nasal, sputum or stools samples to ensure safe collection, handling, and processing plan is in place**
4. **Suggest addressing the current health of the subject before commencing face-to-face research via questions below:**
    - **Have you or anyone in your household tested positive or had a fever, chills, cough, shortness of breath, diarrhea, nausea, vomiting, recent loss of taste or smell, tiredness or fatigue, or muscle aches? If yes, the monitor will not be allowed on campus.**
    - **Have you recently traveled to an area with a widespread outbreak or had close contact with a person known to have COVID-19, MERs-CoV or Ebola?**
    - **Have you traveled outside of the country within the past month? If so, where did you travel and when did you return?**
    - **Have you had a recent SARS-COV-2 antibody test or nasal swab and if so when and what were the results?**

♦ I acknowledge this requirement.