Informed Consent Form for the Study

Temporal Nature of Cognitive and Visuospatial Brain Domain Changes During Long-Duration Low-Earth Orbit Missions (Spatial Cognition)

NASA Grant 80NSSC19K1046
NASA Johnson Space Center IRB Protocol STUDY00000175

Date Approved: 1/12/2021

NASA INSTITUTIONAL REVIEW BOARD (IRB)
CONSENT TO BE A PART OF A RESEARCH STUDY

NOTE: Any alterations to this consent document will invalidate the test subjects' consent unless the changes are approved in advance by the IRB.

ABOUT THIS RESEARCHCONSENT FORM

You may be eligible to take part in a research study.

A research study is carefully planned and designed to increase scientific knowledge.

This NASA IRB Consent form describes important information related to participation in a research study including the purpose, planned procedures, and potential risks.

Please take time to review this information carefully. Talk to the researchers about the study and ask any questions you have. **Make sure you fully understand what will be expected of you and the risks associated with participating in this study.** You may also wish to talk to others (for example, your friends, family, or doctors) about your participation in this study. If and when you decide to be a participant, you will be asked to sign this form and you will be given a copy.

Taking part in this study is completely **voluntary**. The decision to participate is yours. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you.

This NASA IRB Consent form provides a detailed description regarding essential information including, but not limited to, **how, when, where**, and **by whom** a signed informed consent will be obtained.

Note: Failure to disclose pre-existing medical conditions may place you at greater risk for injury or other adverse events resulting from your participation in this study.

1. GENERAL INFORMATION

1.1 Your study title is:
'Temporal Nature of Cognitive and Visuospatial Brain Domain Changes During Long-Duration Low-Earth Orbit Missions (Spatial Cognition)'

1.2 Your study team includes a Principal Investigator, Co-Investigator, Key-Personnel (names, degrees, affiliations):

Co-Principal Investigator: Mathias Basner, MD, PhD, MSc; University of Pennsylvania, USA
Co-Principal Investigator: Alexander Christoph Stahn, PhD; Charité University Medicine Berlin, Germany
Co-Investigator: Diana Arias, MSc; NASA Johnson Space Center, USA
Co-Investigator: Suzanne Bell, PhD; NASA Johnson Space Center, USA
Co-Investigator: Stéphane Besnard, MD, PhD; Université de Caen Basse-Normandie/INSERM, France
Co-Investigator: Katharina Brauns, MSc; Charité University Medicine Berlin, Germany
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Co-Investigator: Tom Hartley, PhD; University of York, UK
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Co-Investigator: Bernhard Riecke, PhD; Simon Fraser University, Canada
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Co-Investigator: Mathias Stangl, PhD; University of California, USA
Co-Investigator: Michael Smith, PhD, MSc; University of Pennsylvania, USA
Co-Investigator: Anika Werner, MSc; Charité University Medicine Berlin, Germany
Co-Investigator: Thomas Wolbers, PhD; German Center for Neurodegengerative Diseases–Magdeburg, Germany
Technical Personnel: Adrian Ecker; University of Pennsylvania, USA
Technical Personnel: Kia Howard; University of Pennsylvania, USA

1.3 This study is sponsored or funded by:
National Aeronautics and Space Administration (NASA) / European Space Agency (ESA) / German Aerospace Agency (DLR)

1.4 Key Information:
This study investigates how brain and behavior are affected by 2-, 6-, and 12-month ISS missions. Brain structure and function will be assessed with magnetic resonance imaging (MRI). Behavior will be assessed surveys and cognitive tests perfomrmed pre-, in-, and post-flight. We will also draw blood to assess biochemical markers of stress and brain changes to investigate the mechanisms underlying any observed changes in brain structure or behavior. Each astronaut will primarily serve as her or his own control, but we also plan comparisons to existing data and data to be collected in non-astronaut control subjects. The study poses minimal risks to participating astronauts.

2. PURPOSE OF THIS STUDY (History and Background)

2.1 You are being asked to join this study because:
Successful human space exploration depends on the integrity of a range of cognitive abilities. In addition to the physiological effects of microgravity, spaceflight involves exposure to multiple environmental (e.g., radiation) and psychological stressors related to living in an isolated, confined, and extreme (ICE) environment that have the potential to degrade astronaut cognitive performance and jeopardize mission success. On the first human mission to Mars, astronauts will spend unprecedented times in space beyond low earth orbit. Our knowledge on how humans will cope with living for prolonged periods of time in an ICE environment is extremely limited (only 4 humans have spent consecutively more than 1 year in space). Studies investigating the neurocognitive effects of living in ICE environments beyond the standard 6-month ISS mission are therefore critically needed to (1) understand the effects on brain structure and function, (2) demonstrate and verify the techniques needed to monitor, diagnose, and prevent such effects, (3) establish a baseline for proposed Deep Space Gateway expeditions of up to 7 months and up to 400 days in the Deep Space Transport, and (4) allow for the confident prediction of adverse effects on astronaut performance out to two to three years of typical Mars conjunction-class missions. The data we propose to collect will - for the first time - reliably demonstrate whether prolonging mission duration to one year will have detrimental effects on general cognitive performance, spatial cognition and brain plasticity relative to the shorter 6-month and 2-month missions, and provide insights on the underlying biological mechanisms.

3. STUDY PARTICIPANTS

3.1 In order to be eligible to participate, you may be asked to undergo the following screening tests or procedures:
In addition to your annual physical examination for flight personnel, you will be asked to complete a questionnaire, which determines your eligibility for magnetic resonance imaging (MRI). Any of the following conditions may exclude you from participation in the study or require additional examinations to perform the

MRI scan: Tinnitus; sensorineural hearing loss > 30 dB; pace maker or internal defibrillator; metallic implants (e.g. orthopedic plates after bone fractures, joint replacements, surgical staples or clips, artificial heart valves, stents, cava filters); metallic splinters (e.g. after an accident or due to war injury); non-removable dental brace; Tattoo (some tattoo inks contain metallic particles); permanent make-up; intrauterine contraceptive device; cochlear implant (implanted hearing device); medication pump; acupuncture needle; other foreign bodies/objects which are non-removable; pregnancy (or its possibility); previous brain and/or heart surgery. Alternatively, you are one of 6 astronauts that have performed the Cognition battery during their 6-month or 12-month ISS mission.

3.2 If you are an astronaut, you are in one of the following three groups:
Group 1: 10 astronauts on 1- to 2-month ISS missions
Group 2: 10 astronauts on a 6-month ISS mission
Group 3: 10 astronauts on a 12-month ISS mission

If you are a control subject, you are in one of the following three groups:
Group 1: 10 control subjects investigated on the ground only like astronauts on 1- to 2-month ISS missions
Group 2: 10 control subjects investigated on the ground only like astronauts on a 6-month ISS mission
Group 3: 10 control subjects investigated on the ground only like astronauts on a 12-month ISS mission

You may also be one of 6 astronauts that have already gathered Cognition data during a 6- or 12-month ISS mission. We will use these data for a normative Cognition database.

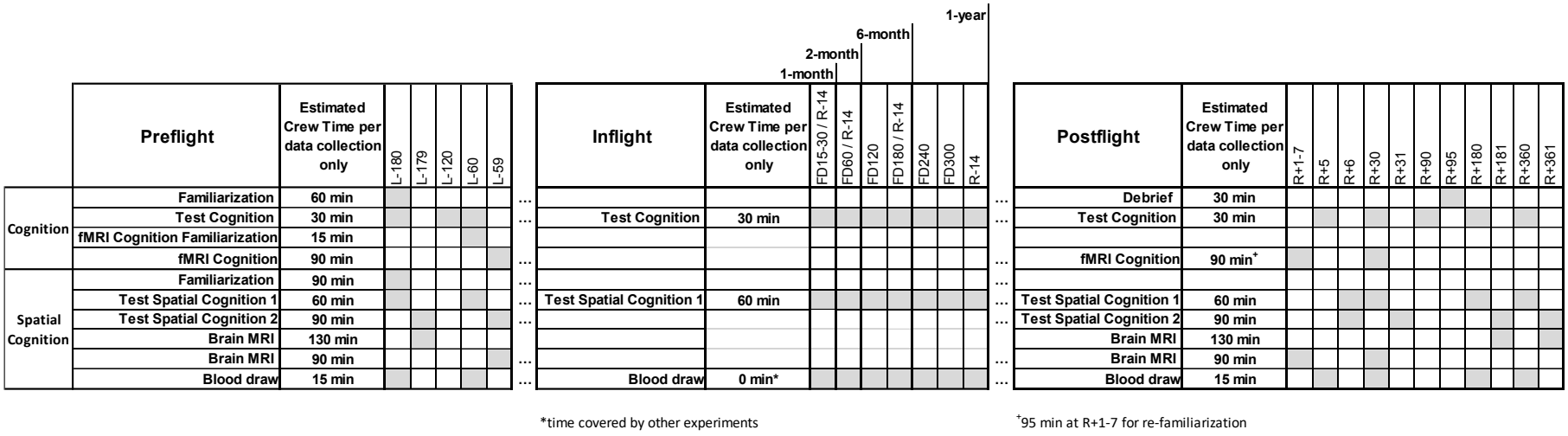
4. STUDY DESCRIPTION

4.1 In this section you are provided a study description in layman's terms that you should easily understand and that provides you the following as applicable: a detailed explanation of each test, including what data will be collected and what equipment will be used; the amount of time each test will take; the frequency of testing, and whether testing is continuous or intermittent; a chart or calendar as a possible addition to the explanation of the tests; the study's duration and when it will be completed; any need for follow-up examinations or tests; the location of the testing; the amount of blood, urine, saliva, other biological samples and/or tissue that will be taken and how often; whether joining this study limits your chance to join other studies; whether "standard" medical procedures are included in the study; how your other activities may be affected by the study (exercise, diet, medications, physical activities, etc.); and a detailed list of any data that have been collected by other means that will be used by or shared with this study.

Overview

'Spatial Cognition' foresees to perform magnetic resonance imaging (MRI) of your brain before and after spaceflight, and cognitive testing and blood draws before, during, and after spaceflight. A summary of the schedule is provided below (Figure 1). Details on each testing day are given in the following subsections. Similar procedures will be performed in up to 30 control subjects going about their normal lives on Earth. Each control subject will be matched on the basis of age, gender and educational background. One specific aim of the study is to generate a normative database for performance on the Cognition test battery during 2-, 6-, or 12-month missions. If you are one of six astronauts that have performed Cognition regularly during your ISS mission, this project asks you to allow us to use your Cognition test data for the normative database. In this case, no new data will be collected from you.

Figure 1: Sessions overview for pre-, in- and post-flight (L=Launch; FD=Flight-day, R=Return). In-flight reserve sessions for Cognition at FD 90, 150, 210, 270, 330 are not shown.



	Preflight	Estimated Crew Time per data collection only	L-180	L-179	L-120	L-60	L-59	...	Inflight	Estimated Crew Time per data collection only	FD15-30 / R-14 (1-month)	FD60 / R-14 (2-month)	FD120	FD180 / R-14	FD240 (6-month)	FD300	R-14 (1-year)	...	Postflight	Estimated Crew Time per data collection only	R+1-7	R+5	R+6	R+30	R+31	R+90	R+95	R+180	R+181	R+360	R+361
Cognition	Familiarization	60 min						...										...	Debrief	30 min											
	Test Cognition	30 min						...	Test Cognition	30 min								...	Test Cognition	30 min											
	fMRI Cognition Familiarization	15 min																													
	fMRI Cognition	90 min						...										...	fMRI Cognition	90 min+											
Spatial Cognition	Familiarization	90 min						...										...													
	Test Spatial Cognition 1	60 min						...	Test Spatial Cognition 1	60 min								...	Test Spatial Cognition 1	60 min											
	Test Spatial Cognition 2	90 min						...										...	Test Spatial Cognition 2	90 min											
	Brain MRI	130 min																	Brain MRI	130 min											
	Brain MRI	90 min						...										...	Brain MRI	90 min											
	Blood draw	15 min						...	Blood draw	0 min*								...	Blood draw	15 min											

*time covered by other experiments

+95 min at R+1-7 for re-familiarization

(1) Magnetic resonance imaging (MRI): You will take part in several MRI scanning sessions of your brain (up to 6 sessions, as depicted in Figure 1). MRI scanning will be used to measure your brain activation patterns while you are resting and performing various tasks. This will provide us with information about the brain's structure and function. Prior to testing you will complete several questionnaires about your eligibility for MRI scanning. In addition, you will complete a survey about your handedness. During the scanning procedure, you will be lying inside a strong magnetic bore (a standard clinical MRI scanner) that makes noisy beeping and hammering sounds. Disposable earplugs or ear-bud headphones will be provided to diminish the noise. The procedure is painless and does not put you in any danger. However, you are not allowed to have any metal objects with you while in the MRI scanner room. You will be asked to lie down on a platform, which can be slid into the middle of the magnet, which is shaped like a large tube. An MRI imaging coil will be placed around your head. You will not come into contact with the coil during the experiment. Foam pads will be placed around your head to limit head movement during the measurements. You will then be slid into the magnet. You will be asked to lie still for up to 1.5 hours, during which time several MRI scans will be acquired. During a few of the scans you will be asked to perform computer tasks. During some of the scans you will be asked to do nothing but lie still in the scanner and remain awake. If you feel claustrophobic, or excessively uncomfortable inside the scanner, we will remove you from the environment immediately upon your request. The total administration time for this test is about 90 min per session. There will be additional travelling time to the MRI facilities is about 15 min from NASA Johnson Space Center. MRI testing is performed two times before and up to four times after the mission.

(2) Cognitive Performance: You will perform three test batteries behavioral tests for assessing your cognitive performance. The tests of the first battery called *Cognition* are performed four times (including a familiarization) before the mission, up to 12 times during the mission (one time for 1-month crews, two times for 2-month crews, as many as six times for 6-month crews, and up to 12 times for 12-month crews), and five times after the mission. The tests of the second test battery, *Spatial Cognition 1*, are performed three times (including a familiarization) before the mission, up to seven times during the mission (one time for 1-month crews, two times for 2-month crews, four times for 6-month crews, and seven times for 12-month crews), and four times after the mission. The third test battery, *Spatial Cognition 2*, will be performed only on-ground, three times before (including one familiarization) and four times after the mission. To account for any changes in mood, fatigue and well-being, affective states will be determined prior to the start of cognitive testing using visual analogue scales (VAS). Some tests may also require you to rate the level of difficulty of the tasks. Finally, as part of these tests you will also be asked to complete a questionnaire on your computer experience as well as your sense of direction, and perform a structured interview on your spatial cognitive abilities. A summary describing each of the tasks is provided on the following page (Table 1).

(3) Blood draw: You will also be asked for blood samples (about 7.5 ml blood) two times before the flight, up to seven times during the mission, and four times after the mission (up to 13 times in total). The total maximum of blood needed is about 100 ml. These samples can be used to determine biochemical factors related to any structural and/or functional changes of your brain, such as neurotrophic factors, growth factors, and inflammatory responses. Blood draws should be performed at the same time of the day in the morning after an overnight fast. All samples will be labeled with your ID number and only accessible by research staff. Blood draws will typically be combined with those for other studies.

Your total time commitment is expected to be approximately 42 hours for 1-month crews, 45 hours for 2-months crews, 51-52 hours (depending on the number of reserve sessions) for 6-months crews, and 60-62 hours (depending on the number of reserve sessions) for 12-months crews. Actual time may be less due to efficiencies with other studies within the complement.

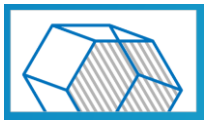
Table 1: *Test Batteries 1 and 2 composition and definition. It does not include the level of computer experience survey, as this will be filled in only once, outside the test batteries.*

Test Battery 1 & 2	
Visual Analogue Scales (VAS)	*Purpose*: To assess mood, fatigue and sleep *Description*: To assess mood, fatigue and sleep, affective states, visual analogue scales (VAS) will be used with the following binary anchors: happy – unhappy; healthy – sick; energetic – physically exhausted; mentally sharp – mentally fatigued; not stressed – very stressed; fresh/ready to go – tired; good sleep quality – poor sleep quality; and high workload – low workload; very depressed – no depressed at all; not lonely at all – very lonely; motion sick – not motion sick at all; you will also be asked to indicate when you were to sleep and when you woke up as well as whether you had a conflict with another crewmember in the past week, and whether it was solved.
Test Battery 1	
Spatial Updating	*Purpose:* To assess spatial updating *Description*: You initially have to encode the position of an object presented at unpredictable positions in a virtual environment. The object then gradually disappears, followed by a static or dynamic delay phase. In the dynamic delay phase you will experience a virtual forward translation and rotation, after which you have to point toward the remembered location of the object. In contrast, in the static delay phase you remain stationary instead of moving forward, thus requiring you to point toward the original location of the target object at retrieval.
Four Mountains Task	*Purpose:* To assess topographical memory *Description*: To specifically target topographical memory, a version of the Four Mountains Task will be performed. You will be asked to briefly study a landscape scene. Subsequently, you will be shown several variations of the previously displayed scene from a novel viewpoint and under altered non-spatial conditions and you have to identify, which of these scenes is identical to the one that was initially presented.
Point to Origin Task	*Purpose*: To assess path integration *Description*: A sparse visual flow is presented on a screen to you, and supported by auditory information. At the end of each path, you will be asked to point back to the origin by rotating an arrow. In addition, you will also have to estimate the distance of the homing vector (linear distance to the point of origin). After each trial, you will be asked to rate the level of difficulty of the trial.
Navigation Search	*Purpose:* To assess spatial memory and spatial updating *Description:* You will be shown a virtual environment that contains a number of boxes. Some of the boxes contain a target, which can only be seen when the box is approached from the front to a close distance. The task is to locate and collect all targets as quickly as possible. Each session the task will be performed in two different conditions, differing in their background (night vs. day). On-ground the task will also be administered with a head mounted display and controllers, while moving in a small circular area (radius: 2 m).

Test Battery 2	
Perspective Taking	*Purpose*: To assess spatial orientation ability, i.e. the ability to occupy new imaginary positions within a configuration of objects *Description*: A picture with several objects is displayed on a screen. On each item, youare asked to imagine being at the position of one object in the display (the station point) facing another object (defining their imagined heading or perspective within the array) and are asked to indicate the direction to a third (target) object.
Virtual Mazes	*Purpose*: To assess spatial navigation *Description*: This test comprises several tasks. During each task a 3D environment is presented to you from a first-person perspective. You are then asked to move to a target using different cues, starting from different positions as quickly as possible. You may perform variations of this task during preflight- and postflight testing, including different environments and set ups, and complete questions about your strategies.
Cognitive Mapping Task	*Purpose:* To assess spatial memory formation *Description*: You will be asked to first learn a route through a novel virtual large realistic environment, consisting of a network of paths, non-specific buildings, and distinctive landmarks. You are instructed that you are required to learn a long, indirect route through the environment and will be asked to provide directions during a subsequent probe trial. Following the completion of the learning phase, you will be asked to perform a cognitive map test by indicating spatial relationships between two specific landmarks encountered along the route during the learning phase. Importantly, the target landmark is never visible from the respective trial location. The pointing error between the correct direction and estimated direction between the current location and the target landmark will be used to quantify spatial memory. After completion of the task you will perform a debriefing questionnaire about your sense of direction and a survey about your response strategies. You may perform variations of this task pre- and postflight.

The Cognition test battery consists of the following 10 cognitive test:

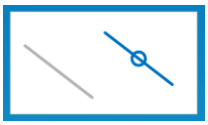
The **Motor Praxis** Test is a measure of ***sensory-motor speed*** and projects to the sensorimotor cortex.[65] You have to mouse click on ever-shrinking blue boxes that appear in varying locations on the screen.



The **Visual Object Learning** Test is a measure of ***visual object learning and memory*** and projects to the medial temporal cortex and the hippocampus.[66] You have to remember and later recall ten 3D Euclidean shapes.

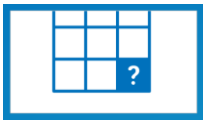
The **Fractal-2-Back** is a measure of ***attention and working memory*** and projects to the dorsolateral prefrontal cortex, cingulate cortex, and Hippocampus.[67] You are asked to press the spacebar whenever the fractal on the screen is the same as the fractal before the previous one.

The **Abstract Matching** Test is a measure of ***visual abstraction*** and projects to the prefrontal cortex.[68] You are asked to pair a central target object with two objects on either the left or right lower side of the screen.



The **Line Orientation** Test is a measure of ***spatial orientation ability***, based on Benton's test, and projects to the right temporo-parietal cortex and the visual cortex.[69] In each trial, you are asked to rotate a moveable blue line of variable length so that it is parallel to a fixed black line.

The **Emotion Recognition** Test projects to the cingulate cortex, Amygdala, Hippocampus, and fusiform face area.[70, 71] You are shown a series of faces and asked to determine what emotion the face is showing: happy, sad, anger, fear or no emotion. Difficulty is varied by emotion intensity.



The **Matrix Reasoning** Test is a measure of ***abstract reasoning*** and consists of increasingly difficult pattern matching tasks.[65, 72] It is analogous to Raven Progressive Matrices[73] and projects to prefrontal, parietal, and temporal cortices.[72]

The **Digit Symbol Substitution** Test involves matching numbers to symbols and is a measure of ***complex scanning, visual tracking, and attention***.[74-76] It is part of WinSCAT and projects to temporal, prefrontal, and motor cortices.

The **Balloon Analog Risk** Test is a measure of ***risk decision making*** and projects to the orbital frontal cortex, amygdala, hippocampus, and anterior cingulate cortex.[77] You bet by inflating 30 computerized balloons, with larger balloons offering greater but riskier rewards.

The 3-min. **Psychomotor Vigilance** Test measures ***vigilant attention*** by recording reaction times to visual stimuli that occur at random inter-stimulus intervals.[34, 78-83] It projects to prefrontal, motor, and visual cortices.

Training and Ground Sessions Location

Experiment training for 'Spatial Cognition' is planned to be conducted at the European Astronaut Center (EAC) in Cologne, Germany and/or at NASA-JSC. The training will cover all required operations for data collection, data download, and potential malfunction. The pre-flight and post-flight brain imaging are expected to take place at NASA-JSC in Houston in close collaboration with the University of Texas Medical Branch (UTMB) at Victory Lakes.

Data Sharing

This study is part of a complement of interrelated studies that will be implemented as one study.

This specific investigation is requesting data from the following other investigations in this complement or from other experiments collecting as defined in the crew's individual Data Sharing Plans:

Standard Measures (Pro2231, PI: Clement):
- Cognition
- Blood (Insulin-like growth factor 1, Vascular endothelial growth factor)
- Cellular profile
- Actigraphy
- Biochemical Markers
- Microbiome
- Sleep
- Sensorimotor

NINSCAN (STUDY00000247, PI: Zhang):
- Blood (Brain-derived neurotrophic factor)

This specific investigation is also requesting the following from Medical Operations (MEDB):
- T1 and T2 weighted structural scans, DTI Sequence (Med Ops MRI, MEDB 1.10)
- WinSCAT (Med Ops, MEDB 7.4)
- Radiation - Personal Dosimetry (Med Ops, MEDB 3.1)
- Exercise Logs (Med Ops, ASCR Exercise, MEDB5.2)
- Medication Logs (Med Ops, MEDB 1.1/1.3)
- Clinical Lab Assessment (Med Ops, MEDB 2.1)
- Physical Fitness Evaluation: Functional Fitness (Med Ops, MEDB 5.1)

- Cycle Ergometer/Aerobic Functional Capacity (Med Ops, MEDBN 3.07)

This specific investigation is also requesting the following Environmental/ECLSS variables:
- CO_2 Levels
- Radiation - Station Level
- Ambient Temperature
- Humidity
- Air Pressure
- O_2 Levels

This specific investigation is also requesting the blood draw spreadsheet and the timeline from day before until end of each session from ROI.

Session Constraints
For excellent data quality, few session constraints few session constraints regarding EVAs, physical activity, fasting, sleep shift and caffeine and alcohol consumption and other cognitive tests not related to 'Spatial Cognition' shall be taken into account. These will be coordinated with you and/or resolved by planning of your sessions.

4.2 You are being told if the study you are joining includes one of the following categories:

☐ *"Randomized"* means that you are put into a study group by chance (e.g., like flipping a coin). Neither you nor the principal investigator will choose what study group you will be in. You will have a chance of being placed in any study group.

☐ *"Blinded"* means you will not know what study group you are in.

☐ *"Double-Blinded"* means that neither you nor the Principal Investigator (double-blinded) will know what study group you are in.

☐ *"Placebo"* means a pill with no medicine. In a placebo-controlled study, you may be given a study medication and it will contain either (name of drug) or placebo (pills with no medicine).

☒ *"Not Applicable"*

5. DRUGS, BIOLOGICS or NEWMEDICAL DEVICES or PRODUCTS

In this section you are being told whether the study uses any drugs, blood or blood components, allergenic substances, vaccines, investigational new medical devices or other similar products used to investigate human anatomy or physiology or to prevent or treat disease or injury.

__X__No study drug, biologic, or investigational new medical device or product will be used.

_____Yes, the study drug, biologic, and/or investigational new medical device or product is:

_____.

If "Yes" is checked above, then the investigator(s) will also provide you with a description of the drug or other substance and/or investigational new device. For investigational new drugs or devices, the investigator will also provide you with any relevant investigational regulatory approval number(s). In all cases the investigator(s) will also provide you with any other materials you require to best assist you with making an appropriately informed decision regarding your participation.

6. INFORMATION ABOUT RISKS AND HAZARDS

6.1 You are joining a study that is:

☒ "Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

☐ "Reasonable risk" means that the probability and magnitude of harm or discomfort anticipated in the research are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, but that the risks of harm or discomfort are considered to be acceptable when weighed against the anticipated benefits and the importance of the knowledge to be gained from the research.

6.2 Hazards represent conditions that have the potential to cause harm. Risks, in turn, originate from hazards. For example "A wet deck on a boat" is a hazard, whereas potential risks associated with that hazard might include slipping and falling down or overboard.

6.3 The risks of joining the study and the steps taken to protect against harm include:

(1) Risk of injuries related to impact of hitting object in MRI
(2) Risk associated with feeling uncomfortable or claustrophobic while inside the MRI magnet.
(3) Risk of an unexpected abnormality being observed in a specific subject's MRI scans, even though scans are not intended for diagnostic purposes. These abnormalities are termed "incidental findings."
(4) Subject discomfort because of noise while lying in MRI.
(5) Unknown risks related to exposure to magnetic field in MRI scanner. The levels of energy used to make magnetic resonance measurements are far less than are used in a single X-ray, and many patients have been safely studied using magnetic resonance techniques. Although there are no known risks of MRI on pregnant women or a fetus, there is a possibility of yet undiscovered pregnancy related risks.
(6) There may be some discomfort associated with the collection of the blood samples, including possible bruising of the arm, redness, swelling around the site, bleeding at the site, dizziness, fainting, sweating, coldness of skin, numbness and tingling of hands and feet, nausea, vomiting, possible visual disturbance, syncope and injury fall from fainting. In some cases, more than one venipuncture may be necessary. Rare adverse effects include thrombosis of the vein due to trauma and infection which results in thrombophlebitis.
(7) In rare cases, subjects may develop a headache or motion sickness and/or experience stress during cognitive testing due to the amount of computer work and/or moving in 3D environments.

6.4 The hazards and the steps used to minimize the hazards include:

(1) Metallic object flying through the air toward the MRI magnet: We require that all people involved with the study remove all metal from their clothing and all metal objects from their pockets. No metal objects are allowed to be brought into the magnet room at any time. In addition, once you are in the magnet, the door to the room will be closed so that no one inadvertently walks into the magnet room.
(2) Small volume of the bore of the magnet in MRI scanner: If you become uncomfortable inside the magnet, you may withdraw immediately from the study. You will be able to talk to the operator throughout the study via intercom, and will be able to let us know right away if you want to stop the study and get out of the scanner.
(3) Incidental findings related to MRI scanning: Most incidental findings have no significant health consequences, but in a small percentage of cases further evaluation or treatment may be indicated. If an incidental finding is noted in a subject's MRI data, the subject will be notified and given a written report describing it. It will then be up to the subject to pursue it with his/her physician. Although study personnel may be able to provide some advice, the decision of whether and how to pursue an incidental finding can only be made by the subject's physician who has knowledge of the subject's medical history.
(4) Loud noise while in MRI scanner: You will wear foam earplugs and / or headphones to reduce the loud noises made by the scanner.

(5) Exposure to strong magnetic field: Pregnant women and/or people with pacemakers, certain metallic implants, or metal in the eye cannot participate in this study. Subjects will undergo a checklist before entering the MRI room to verify that they do not have anything harmful in or on their body.
(6) Venipuncture: To minimize any risk associated with venipuncture, sterile disposable hardware will be used. On-ground experienced technical personnel will perform all procedures. In the event of fainting during the blood draw procedure, a medical evaluation by a physician will be performed. Food and drink will be available.
(7) Performing cognitive tasks: If you feel motion sick, get a headache, feel upset and/or stressed while participating in the computerized tasks, you may immediately pause and/or skip the task. Should you feel that you are unable to complete the task during the course of the study, you are free to withdraw their consent to participate in this experiment.

7. TREATMENT, INJURY AND COMPENSATION INFORMATION

Even though the investigators have taken steps to minimize the risks, you may experience problems or side effects. Therefore the following statement applies for you the participant: "In the event of injury resulting from this study, I understand that I will receive medical attention and available treatment. I also understand that I will be compensated for any injuries to the extent permitted under the laws and regulations applicable to me and the provisions of the contract between me and NASA/ESA/DLR. My agreement to participate shall not be construed as a release of liability which may arise from or in connection with the above procedures for NASA/ESA/DLR or any third party.

8. BENEFITS INFORMATION

8.1 Potential benefits to You: Participation in NASA/ESA/DLR studies generally result in no direct benefit to you as an individual. It is hoped that the information learned from this research study will help the international science partners learn more about human physiological changes for future space flight missions.

8.2 Potential benefits to the Researchers: The research team will utilize this section to inform you whether any member of the research team might potentially receive additional financial or other benefits through the conduct of this research, for example through his/her business affiliations, holdings of stocks or other securities, patents or patent applications, trademarks or trademark applications, etc.

__X__The researchers declare that they have no otherwise undisclosed potential financial benefits.

_____Potential additional financial benefits to the researchers are (include researcher name(s) and nature of benefit(s)):_____
_____.

9. NEW FINDINGS

9.1 If new information is obtained during the study after you have joined, you will be informed. You may change your mind about continuing in the study. You may be asked to sign a new consent form that includes the new information.

10. STUDY WITHDRAWAL and/or TERMINATION

10.1 You may withdraw from the study at any time. If you decide to leave before the study is finished, please tell the investigator or study staff. Your withdrawal could have undesired consequences for your health and/or the health of other subjects. A responsible physician will tell you if there could be any harm to you if you decide to leave before the study is finished. If you tell the researchers your reasons for leaving the study, that information will be part of the study record.

10.2 Your withdrawal or refusal to participate in the study will not result in any penalty or loss of benefits to which you are otherwise entitled.

10.3 If you decide not to join the study, or to withdraw from it you may nevertheless be eligible to participate in other studies.

10.4 Researchers may need to stop your participation in the study even if you want to continue participation. The research may also be stopped at any time by: the Human Research Multilateral Review Board (HRMRB), the Crew Surgeon or other assigned medical monitor, the Flight Director, or the ISS Commander, as appropriate, if the research would endanger any ISS Crew Member, including you, otherwise threaten the mission success, or for any other reason. Some examples of possible reasons include:

- The researcher believes that it is not in your best interest to stay in the study
- Any problem with following study related instructions
- Any problem with following clinic or laboratory policies and procedures
- Any serious complication during the study
- Inappropriate behavior
- The study is suspended or canceled
- The subject's information is or becomes unusable for any reason
- Events beyond the participating agencies' control occur, for example: fire, explosion, disease, weather, floods, terrorism, wars, insurrection, civil strife, riots, government action, or failure of utilities
- Existing data reveal answers earlier than expected

11. COST and FINANCIAL INFORMATION

11.1 There are no costs or bills to you for participation in this study.
11.2 Control subjects will be numerated according to standard policies for participation suggested by FAP/BHP and/or ESA/DLR Standard policies, if applicable.

12. PAYMENT and REIMBURSEMENT

___ **Check here if Section 12.1 is Not Applicable**

12.1 You will be paid to participate in the study as follows:

___ You will not receive payment if you are a NASA civil servant, other federal civil servant employee, contractor, or International Partner crewmember participating in ESA, JAXA, CSA, or NASA-sponsored studies.

If none of the above apply to you, you will receive $10 per hour

13. SUBJECT RECORD CONFIDENTIALITY AND AUTHORIZATION TO RELEASE PROTECTED HEALTH INFORMATION (PHI)

13.1 Your privacy and the confidentiality of data collected or used as a part of this research study will be protected from unauthorized disclosure according to applicable law.

13.2 Your protected health information (such as name, geographic identifier, dates, phone number) may be used or shared by NASA/ESA/DLR offices of research oversight or quality assurance, medical monitors, and researchers for the reasons below:

- To conduct and oversee the research;
- To make sure the research meets NASA/ESA/DLR requirements;
- To conduct monitoring activities (including situations where you or others may be at risk of harm or reporting of adverse events);
- To become part of your medical record if necessary for your medical care;
- To review the safety of the research.
- To support operational clinical activities where clinical experts evaluate relevant medical and research data to recommend clinical practice guidelines or medical requirements specifically for space flight. These data will not include names although other information may implicitly link the information to you.

13.3 For the purposes of ensuring the safety of the study and yourself, and of verifying compliance with applicable laws and regulations, information about you, including protected health information, may be used or seen by the researchers or others, on a need-to-know basis, during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The participating agencies and other government officials may need the information to make sure that the study is performed in a safe and proper manner.
- Other officials may need to review the information if the study involves the use of an experimental drug or device.
- Safety monitors, medical personnel, or safety committees may review your research data, stored biospecimens and/or medical records for the purposes of medical safety, for verification of research procedures, or if any injuries or other adverse events occur.
- A data and safety monitoring board (DSMB) may oversee the research, if applicable.

13.4 In addition to the cases mentioned in 12.2 and 12.3 above, your protected health information obtained through this research may be used or shared with others through separate Data Sharing Agreements to which you yourself have also concurred beforehand by providing a separate signature. The results may be used by the research team and possibly be presented/published in journals or at scientific conferences, but in such cases will not include information that could identify you, directly or by inference, without your consent.

13.5 You have the right to withdraw your consent for the researchers to use or share your protected health information. The researchers will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or to ensure quality of the study. To withdraw your consent, you must submit a written request to do so to the researcher and, if relevant, the Data Sharing Agreement administrator.

13.6 You have the right to request access to your study records after the study is completed. To request this information, you must do so in writing by contacting the researcher. Should your personal data in those study records be incorrect, you have the right to request that this be corrected.

13.7 Any data (including but not limited to standard measures, laboratory data, psychological, or physiological measurements) or biospecimens obtained from you for this research study may become part of the participating agencies' archives, based on each specific agency's arrangements with their investigators. These data or biospecimens may be used for future research. For de-identified data or biospecimens additional informed consent is not needed unless your consent is required by your primary Agency. All applicable laws, regulations, and policies concerning the privacy and confidentiality of these data will be followed. Records or biospecimens stored in these archives will not be released or used in a way that identifies you by name – a code will be assigned. However, records or biospecimens may be implicitly linked to you through fields such as mission duration, gender, age, etc.

14. CONTACT INFORMATION

14.1 You may contact the Co-Principal Investigators to:

- Obtain more information about the study;
- Ask a question about the study procedures;
- Report an illness, injury, or other problem;
- Leave the study before it is finished;
- Express a concern about the study.

Principal Investigator:

Project A

Mathias Basner, MD, PhD, MSc

Email Address: basner@pennmedicine.upenn.edu

Mailing Address: University of Pennsylvania, Dept. Psychiatry, 1019 Blockley Hall, 423 Guardian Dr, PA 19104, USA

Telephone: (+1-215) 573 5866

Project B

Alexander Stahn, PhD

Email Address: alexander.stahn@charite.de

Mailing Address: Charité University Medicine Berlin, Charitéplatz 1, Virchowweg 6, 10117 Berlin, Germany

Telephone: (+49-30) 450 528 553

You may express a concern about this study by contacting the NASA Institutional Review Board (IRB) listed below:

Office of Research Assurance: Research Integrity & Protection of Human Subjects
2101 NASA Parkway
Mail Code SA
Houston, Texas 77058
Telephone: (281) 204-1650
E-mail: NASA-IRB@nasa.gov

15. RECORD of INFORMATION PROVIDED

15.1 Your signature in the next section means that you have received copies of all of the following documents:

- This NASA IRB "Consent to be Part of a Research Study" document;
- Video, Audio, and Photo Consent, as applicable;

  Other (specify): _____

16. SIGNATURES

Research Subject Understanding:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with Dr. Mathias Basner (or Designee) and I hereby give my consent to participate in this study as a research subject. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact the study team. I understand that I will receive a copy of this form at the time I sign it and later upon request.

Signature of Subject: _____ Date: _____

Name (Print legal name): _____

Video, Audio, and Photo:

I understand that this study will utilize video, audio and/or still photography to analyze study results and I consent to the use of these materials.

☐I accept

☐I do not accept

☐Not applicable(study will not utilize video, audio or still photography)

Signature: _____

Principal Investigator (or Designee):

I have given this subject information about this study. I believe this to be accurate and complete. The subject has indicated that he or she understands the nature of the risks and benefits of participating in this study.

Name: _____ Title: _____

Signature: _____	Date: _____

Note:

Principal investigators are required to retain the signed, dated copy of this form with any attachments for at least 3 years beyond the date of the completion of the study.