A Year on the International Space Station: Implementing a Long-Duration Biomedical Research Mission

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INTRODUCTION: The year-long mission of American astronaut Scott Kelly and Russian cosmonaut Mikhail Kornienko included the most complex biomedical experiments ever conducted on the International Space Station—and arguably in human spaceflight—to establish insight into human health risks of interplanetary exploration. Focusing on risk mitigation, NASA conducted investigations that addressed spaceflight health hazards to varying degrees. This pilot mission was initiated to gain further knowledge and monitor the physiological, psychological, and medical effects of long-duration exposure to spaceflight.

METHODS: NASA's Human Research Program and the Russian Academy of Sciences' Institute of Biomedical Problems identified more than 20 biomedical risk-reduction research investigations to be conducted on the two crewmembers before, during, and after their yearlong expedition. A database of results, as well as observations on programmatic resources, was collected to understand essential elements for future spaceflight health studies.

RESULTS: Statistical rigor requires additional testing at a length of 1 yr to demonstrate the presence or absence of unacceptable deleterious effects, and to permit extrapolation to longer durations in space. Review of experimental procedures from this mission suggests potential efficiencies for future investigations.

DISCUSSION: The Kelly-Kornienko 1-yr mission demonstrated the importance of continuing joint investigations with the adoption of standard measures for rigorous comparisons across disparate populations. It identified improvements to collaborative processes across national and international scientific research programs. Additional studies will inform the development of an integrated applied research methodology for the space station and future interplanetary expeditions.

KEYWORDS: Kelly, Kornienko, one-year mission, 1YM, NASA Human Research Program (HRP).

Charles JB, Pietrzyk RA. *A year on the International Space Station: implementing a long-duration biomedical research mission*. Aerosp Med Hum Perform. 2019; 90(1):4–11.

During the past five decades, more than 550 people have traveled into low Earth orbit (and beyond) and returned successfully. Their 1240 flights were as brief as 108 min and as long as 437 d. The majority (80%) of these flights lasted fewer than 30 d, a convenient boundary[9] between "short-duration" and "long-duration" spaceflights.

The remaining 20% of human spaceflights were long-duration missions, mostly aboard the Russian space station Mir or International Space Station (ISS), with "standard" tours of duty of about 6 mo in duration.[13] At time of publication, only eight people had stayed in space for more than 300 consecutive days and none for 438 d or longer (**Table I**).

Prior to 2015, time away from Earth—arguably the most important determinant of astronaut health and safety during a Mars mission—had not been fully explored or wholly understood. In order to guide research and technology development for interplanetary exploration, NASA's Human Research Program (HRP) focused on five fundamental hazards associated with long-duration spaceflight: space radiation, isolation and confinement, distance from Earth, altered gravity fields, and hostile/closed environments. Considering the state of near-term technology, the biomedical effects of these five hazards could be compounded by another element: time.

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This manuscript was received for review in May 2018. It was accepted for publication in October 2018.

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DOI: https://doi.org/10.3357/AMHP.5178.2019

Table I. List of Crewmembers with Spaceflights of Greater Than 300 d.

COSMONAUT	MISSION	LAUNCH DATE	DURATION (DAYS)
Yuri Romanenko	Mir 2-3	1987-02-05	326
Vladimir Titov	Mir 3	1987-12-21	365
Musa Manarov	Mir 3	1987-12-21	365
Sergei Krikalyev	Mir 9-10	1991-05-18	312
Valeri Polyakov	Mir 15-16-17	1994-01-08	438
Sergei Avdeyev	Mir 26-27	1998-08-13	380
Scott Kelly	ISS 43-44-45-46	2015-03-28	340
Mikhail Kornienko	ISS 43-44-45-46	2015-03-28	340

Increased time away from Earth could have dangerous consequences for astronauts already feeling the effects of spaceflight, which range from sensorimotor alterations to possible increases in intracranial pressure. The 400-million km (250-million mi) trek to Mars would require an expedition crew to spend over 2 yr in the extreme environs of space. The duration of a Mars-class mission could, therefore, exacerbate all five hazards of space exploration, highlighting the need for biomedical research to assess whether certain health outcomes worsen over time.

To help bridge this gap in scientific knowledge, the International Space Station Program's five partner space agencies agreed to conduct a "1-yr mission" (1YM) dedicated to the longitudinal study of spaceflight health hazards. A launch date was set for March 2015 and the actual flight duration was set as 340 d due to launch and landing scheduling constraints. The partner agencies formulated several objectives for human research: to gather biomedical data for future long-duration missions; develop capabilities for joint collaborative research in space; and make those capabilities available for all future space station expeditions.

This paper describes the programmatic aspects of preparing for and implementing a unique class of multinational studies in space. It examines 17 scientific investigations conducted in the Kelly-Kornienko 1YM, describing the different aspects of collaborative research between space agencies and the development of joint processes to share equipment and data. The biomedical studies are only briefly summarized, as detailed scientific results will be published separately by the principal investigators. Implications for future investigations and operations are considered.

METHODS

The study protocol was approved in advance by NASA's Johnson Space Center Institutional Review Board. The Institute of Biomedical Problems (IBMP) Bioethics Commission reviewed and approved the Russian 1YM program. The consolidated Human Research Multilateral Review Board (HRMRB) established by the ISS partnership reviewed and approved all 1YM investigations using human subjects. Each subject provided written informed consent before participating.

The ISS partner agencies, working through the Space Station Control Board, designated NASA and the Russian space agency Roscosmos to oversee the Kelly-Kornienko 1YM on the space station. NASA delegated responsibility for American investigations to its Human Research Program and Roscosmos assigned responsibility to the IBMP of the Russian Academy of Sciences. The American and Russian programs began exchanging lists of potential investigations and coordinating plans for collaborative research. Other space agencies, including the Canada Space Agency, the Japanese Aerospace Exploration Agency (JAXA), and the European Space Agency, had the opportunity to propose investigations and conduct concurrent research aboard the space station to augment 1YM data collection. As the European Space Agency is a consortium of 22 member nations, the international representation of the Kelly-Kornienko 1YM is noteworthy.

NASA was interested in comparing physiological, psychological, and performance effects seen at different durations, i.e., 1 yr in space compared to circa 6-mo missions. Results showing meaningful differences between the 6-mo and 1-yr data sets would indicate areas requiring more in-depth investigation. Those with few or no differences would indicate areas where: 1) adjustment to spaceflight could be assumed to be nearly fully established after about 6 mo, with little further change projected on longer missions; or 2) current ameliorative countermeasures were shown to be effective, given present knowledge. It must be noted that the effects of long-term exposure to the radiation environment are still to be determined.

IBMP engaged in a similar process to select the Russian investigations. However, there were important differences between the approach taken by Roscosmos and that taken by NASA. Prior to the Kelly-Kornienko 1YM, Roscosmos had already conducted human spaceflights longer than 9 mo. Furthermore, Russian cosmonauts had routinely repeated investigations on space station missions. As a result, Roscosmos was less compelled to perform duration-specific investigations for the 1YM.

The final set of selected Russian and American investigations was approved by each respective agency's institutional review board and the international HRMRB, responsible for the human safety aspects of ISS biomedical research. NASA's Johnson Space Center Institutional Review Board reviewed and approved the proposed HRP 1YM studies. The IBMP Bioethics Commission reviewed and approved the Russian 1YM program. The consolidated HRMRB established by the ISS partnership reviewed and approved all 1YM investigations using human subjects.

NASA and Roscosmos proceeded to identify subjects and specify investigations that would take place on the space station as part of the 1YM. An American astronaut, Scott Kelly, and a Russian cosmonaut, Mikhail Kornienko, were selected to spend 340 d in space (**Fig. 1**).

Selection of Kelly allowed scientists to compare his physiological and psychological responses during the 1YM with those from a prior 159-d ISS mission. Repetition of five of the investigations from his prior long-duration space station mission permitted direct comparisons, albeit confounded by the unavoidable fact that he was about 10% older for the 1YM

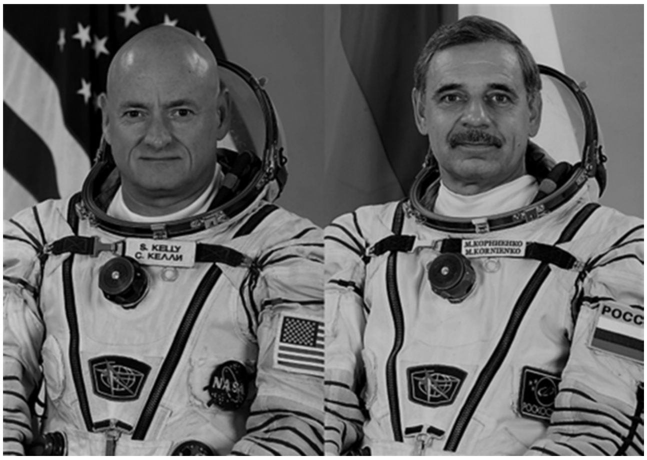

Fig. 1. The crewmembers of the year-long ISS expedition: Scott Kelly and Mikhail Kornienko. Credit: NASA.

(51.1 yr vs. 46.6 yr for his 5-mo mission), and he had the experience of a prior long-duration spaceflight. Kornienko had one prior spaceflight, a long-duration mission of 176 d. Like Kelly, Kornienko was about 10% older when the 1YM launched.

Plans were formulated for integrated procedures and shared resources. Between the United States and Russia, approaches for bilateral collaboration were established: joint investigations with coprincipal investigators from both nations, where crewmembers would be involved in the same investigations; and cross-participation, where astronaut Kelly would take part in a Russian-sponsored investigation and cosmonaut Kornienko would take part in a U.S.-sponsored investigation. Other international space agencies and research communities were given the opportunity to participate through working groups, concurrent research, and data sharing. Finally, the Kelly-Kornienko 1YM studies benefited from coordination of policies, practices, and procedures between NASA's HRP, 1YM researchers, ISS, and ISS Medical Operations. The matrix of multilateral research collaboration achieved during 1YM studies is shown in **Table II**. During the 340 d in space, Kelly also participated in the landmark Twins Study[8] (**Fig. 2**) and several non-NASA 1YM investigations (three sponsored by JAXA[8] and two sponsored by Roscosmos[7]).

Data Collection Sessions

As part of the 1YM, Kelly completed 74 in-orbit data collection sessions, totaling nearly 357 h for 15 in-flight HRP experiments. Kornienko completed 41 in-orbit sessions for six in-flight HRP experiments. A total of 459 biological samples were taken in flight, including approximately 450 mL of blood and 1.3 L of urine.

Table II. List of Research Investigation Titles and Principal Investigators.

INVESTIGATION TITLE	SHORT TITLE	PRINCIPAL INVESTIGATOR
Prospective Observational Study of Ocular Health in ISS Crews.	Ocular Health	Christian Otto,*[14] (Ocular Health) NASA/USRA
Fluid Shifts Before, During, and After Prolonged Space Flight and Their Association with Intracranial Pressure and Visual Impairment.	Fluid Shifts	Michael Stenger, (NASA/Wyle),[24] Scott Dulchavsky (Henry Ford Medical Center),[6] Alan Hargens (University of California at San Diego),[10] Valery Bogomolov (IBMP)
Physiological Factors Contributing to Postflight Changes in Functional Performance.	FTT	Jacob Bloomberg (NASA)[3]
Spaceflight Effects on Neurocognitive Performance: Extent, Longevity, and Neural Bases.	Neuromapping	Rachael Seidler (University of Michigan)[18]
Effects of Long-Duration Microgravity on Fine Motor Skills: 1-yr ISS Investigation.	Fine Motor Skills	Kritina Holden (NASA/Lockheed Martin)[11]
QCT Modality for Risk Surveillance of Bone-Effects of In-Flight Countermeasures on Sub-Regions of the Hip Bone.	Hip QCT	Jean Sibonga (NASA)[19]
Integrated Resistance and Aerobic Training Study.	Sprint	Lori Ploutz-Snyder (NASA/USRA)[16]
Recovery of Functional Sensorimotor Performance Following Long Duration Space Flight.	Field Test	Millard Reschke (NASA),[17] Inessa Kozlovskaya (IBMP)
Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue.	Cognition	Mathias Basner (University of Pennsylvania)[2]
Behavioral Issues Associated with Long Duration Space Missions: Review and Analysis of Astronaut Journals – Extension.	Journals	Jack Stuster (Anacapa Sciences)[25]
Psychomotor Vigilance Test (PVT) on ISS /Reaction Self Test.	PVT/RST	David Dinges (University of Pennsylvania)[5]
Biochemical Profile.	Biochem Profile	Scott Smith (NASA)[21]
Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity.	Salivary Markers	Richard Simpson (University of Houston)[20]
Defining the Relationship Between Biomarkers of Oxidative and Inflammatory Stress and the Risk for Atherosclerosis in Astronauts During and After Long-Duration Spaceflight.	Cardio Ox	Steven Platts (NASA)[15]
Sleep Wake Actigraphy and Light Exposure on ISS12.	Sleep	Laura Barger† (Mass. General Hospital, Brigham and Women's Hospital)[4]
Habitability Assessment of the International Space Station.	Habitability	Sherry Thaxton (NASA/Lockheed Martin)[26]
Study of the Impact of Long-term Space Travel on the Astronaut's Microbiome.	Microbiome	Hernan Lorenzi (J. Craig Vintner Institute)[12]

* Brandon Macias succeeded Christian Otto as Principal Investigator in 2017.
† Laura Barger acted as Principal Investigator.

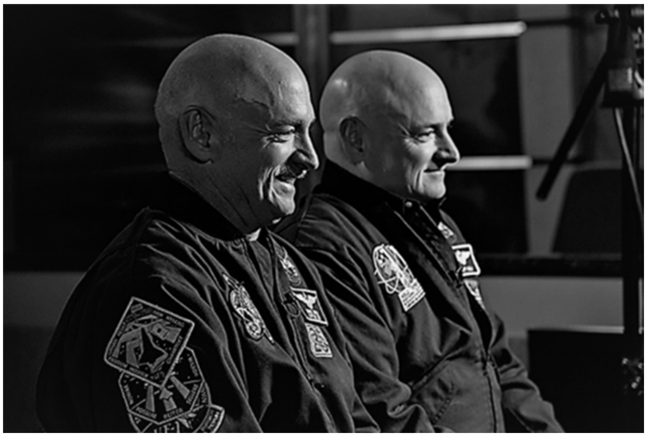

Fig. 2. The subjects in the NASA Twins Study: astronaut Scott Kelly and retired astronaut Mark Kelly. Credit: NASA.

Preflight, in flight, and postflight measurement sessions were scheduled to satisfy the investigators' peer-reviewed requirements, in keeping with the ethical, medical, programmatic, and operational constraints implicit in a complex, multinational undertaking. Preflight measurements were taken to establish baselines under normal conditions on Earth. In-flight data collection was informed by those preflight measurements. Postflight measurements documented the acute residual effects of spaceflight, including the ability to respond to normal gravity after exposure to weightlessness and recovery time needed to restore preflight baseline conditions.

On the Kelly-Kornienko 1YM, as on other spaceflights, investigators requested in-flight measurements to document the time course of a parameter's response to spaceflight factors (e.g., changes to ocular structure as a result of continuous weightlessness). In-flight measurements were scheduled to maximize the efficient use of crew time and spaceflight resources, while minimizing the number of tedious, time-consuming, and complex events that crewmembers underwent such as venipunctures, exercise rounds, or activities requiring coordination with ground controllers and medical monitors. Similarly, preflight measurement sessions had to be coordinated with astronaut travel and training schedules; postflight sessions were scheduled to accommodate recovery, rehabilitation, family, and programmatic demands. A complete list of investigations in the Kelly-Kornienko 1YM is shown in Table II. Studies are shown with full title, short title, and principal investigator name(s).

Operational Constraints

Investigations using ISS crewmembers as participants, and especially as test subjects, face constraints during spaceflight, as well as before and after flight. Each crewmember is responsible for maintaining the numerous complex systems of the space vehicle. Periodically, scheduled research sessions are interrupted by higher-priority activities such as crew transport or cargo vehicle arrival and departure, and extravehicular activities outside the space station. These operational constraints impact data collection sessions, as noted in **Table III**.

Investigations

In addition to NASA HRP investigations and the NASA Twins Study, Kelly participated in several non-NASA 1YM investigations sponsored by JAXA and Roscosmos. Non-HRP studies are not described in this paper. The 17 NASA HRP investigations undertaken during the Kelly-Kornienko 1YM are described in **Table IV**. Short background descriptions are included with each investigation. For the 17 NASA HRP studies, a link is provided to the relevant and mandatory annual reports in the NASA Task Book.[23]

RESULTS

The joint work of this yearlong expedition advanced science and provided valuable input for experimental design of future research in space. Table IV describes research collaboration, joint processes initiated through 1YM collaboration, and implications for future biomedical risk reduction studies in space.

DISCUSSION

The very long expeditions required for human exploration of Mars will expose astronaut crews to known hazards of spaceflight—space radiation, isolation and confinement, distance from Earth, altered gravity, and hostile/closed environments—to a degree never before experienced by humans. Considered in terms of health risk, these hazards will manifest through medical events, diminished physical capacities, and behavior/performance concerns. Preparatory work on the space station can establish the likelihood of medical conditions and other negative events; characterize trends as a function of the age and sex of the astronauts and their time in space; and establish the efficacy of preventive and ameliorative measures.

The goals of the Kelly-Kornienko 1YM were to use the ISS efficiently to reduce human risks of exploration missions beyond low Earth orbit, to renew human space research collaborations between the United States and Russia, and expand collaborative research efforts to include other space station partner members. Certain investigations illuminated the role of cephalad fluid redistribution in near-field vision and evaluated the use of lower body negative pressure as a diagnostic technique and possible countermeasure (**Fig. 3**). Others documented the human capacity for physical performance of postlanding tasks for a mission to Mars.

Overall, the Kelly-Kornienko 1YM identified the importance of continuing joint investigations and adoption of standard measures for rigorous comparisons across disparate populations. It identified key barriers to scientific collaboration that must be overcome to make space station utilization more productive (**Fig. 4**). At the same time, it created a collaborative template for future exploration and international human spaceflight research, and fostered improvements to joint processes for coordinated planning and implementation within existing national research programs.

Table III. HRP Biomedical Investigations in Which Kelly and Kornienko Participated During 1YM.

TITLE (SHORT)	PRIOR PARTICIPATION	COMPLETED DATA COLLECTION SESSIONS	NOTES
Ocular Health	Kelly: N	Consistent with annual schedule of eye exams for ocular health	Ongoing
	Kornienko: N	One session waived; utilized data share from standard medical protocol	
Fluid Shifts	Kelly: N	Completed data sets	First subjects, Joint investigation (NASA and IBMP co-principal investigators)
	Kornienko: N	Incomplete post-flight sessions	
FTT	Kelly: Y	Only Kelly participated All pre- and post-flight testing completed	Reinitiated augmentation; allowed direct comparison with prior long-duration mission
	Kornienko: N		
NeuroMapping	Kelly: N	Only Kelly participated. All scheduled pre-, in- and post-flight testing completed	Ongoing
	Kornienko: N	Incomplete post-flight sessions	
Fine Motor Skills	Kelly: N	Only Kelly participated. Completed data sets	First subjects
	Kornienko: N		
Hip QCT	Kelly: Y	Only Kelly participated. Completed data sets	Reinitiated augmentation; allowed direct comparison with prior long-duration mission
	Kornienko: N		
Sprint	Kelly: N	Only Kelly participated as a Control Two $V\text{O}_2$ exercise sessions and three ultrasounds were not conducted; acceptable reduction	Ongoing Control subject
	Kornienko: N		
Field Test	Kelly: N	All scheduled pre- and post-flight testing was completed as scheduled	Ongoing joint investigation(NASA and IBMP co-principal investigators)
	Kornienko: N	All scheduled pre- and post-flight testing was completed as scheduled	
Cognition	Kelly: N	Pre, post sessions completed, reduced in-flight sessions	Ongoing
	Kornienko: N	Pre, post sessions completed, reduced in-flight sessions	
Journals	Kelly: N	Only Kelly participated.	Reinitiated augmentation; allowed direct comparison with prior long-duration mission
	Kornienko: N		
PVT / RST	Kelly: Y	All objectives planned during mission were accomplished	Reinitiated augmentation; allowed direct comparison with prior long-duration mission
	Kornienko: N	All objectives planned during mission were accomplished	
Biochem Profile	Kelly: Y	Only Kelly participated. Complete pre, in- and post-flight sample collection	Derived from Nutrition Supplemental Medical Objective (SMO)
	Kornienko: N		
Salivary Markers	Kelly: N	Only Kelly participated. Complete pre, in- and post-flight sample collections	Reinitiated augmentation; allowed direct comparison with prior long-duration mission
	Kornienko: N		
Cardio Ox	Kelly: N	Only Kelly participated. Complete pre, in- and post-flight sample collection	Ongoing, testing sessions at R+ 3yr and R+ 5yr
	Kornienko: N		
Sleep	Kelly: Y	Both Kelly and Kornienko were Sleep subjects. Some loss of actigraphy data and sleep logs due to hardware and software technical issues.	Reinitiated augmentation; allowed direct comparison with prior long-duration mission
	Kornienko: Y		
Habitability	Kelly: N	Only Kelly participated. Data loss due to software compatibility issue but resolved and most inflight sessions recovered.	Ongoing
Kornienko: N			
Microbiome	Kelly: N	Only Kelly participated. Frozen and ambient blood samples returned.	Ongoing
	Kornienko: N		

Both the multinational Kelly-Kornienko 1YM research program and its constituent Twins Study were constrained by the small pool of test subjects: two participants. To draw any conclusions about the cumulative effects of exposure to space, it is recommended that research be conducted to observe additional astronauts spending longer durations of time in the space environment. NASA's HRP has a requirement for sufficient crewmember experience at 1 yr in spaceflight to demonstrate, with statistical rigor, the presence or absence of unacceptable deleterious physiological, psychological, and medical effects of spaceflight on human health and performance beyond the predominant experience base of short-duration expeditions, and

Table IV. Description of Kelly-Kornienko NASA HRP-Sponsored Biomedical Investigations and Programmatic Considerations.

SHORT TITLE	DESCRIPTION AND PROGRAMMATIC CONSIDERATIONS
Ocular Health	Gathered physiological data to characterize the risk of visual impairment possibly associated with increased intracranial pressure (ICP). Data collection began 1 yr prior to flight, continued in flight approximately every 30 d, and through to 1 yr postflight, or until any abnormalities associated with the 1YM were resolved.
Fluid Shifts	Measured fluid shifts from lower body to upper body; evaluated the impact these shifts have on fluid pressure in the head and changes to eye structures. Determined if these changes could be predicted based upon crewmember baseline data and responses to acute head-down tilt tests performed before launch. A "flagship investigation" of the Kelly-Kornienko 1YM, the Fluid Shifts study was formed from the combination of three separately reviewed and accepted investigations that were combined to maximize efficiency.
Field Test	Determined sensorimotor and cardiovascular performance, with initial measurements initiated as soon as possible after touchdown on Earth, with one to three immediate follow-up measurements on the day of landing. Successfully performed rigorous and repeatable assessments of typical activities to be executed after a planetary surface landing, such as standing from the seated posture, recovery from a fall, walking with eyes open and closed, moving large objects, etc. The investigation also evaluated NASA's new Gradient Compression Garment in comparison with the standard Russian Kentavr lower body compression garment (Zvezda Research, Development and Production Enterprise, Moscow, Russia). Both were tested as interventions to fluid distribution in space.
FTT	Evaluated astronaut postflight functional performance and related physiological changes through an interdisciplinary testing regimen representative of critical mission tasks. Identified key physiological factors that contribute to functional decrements so that targeted countermeasures can be developed. Data from previous Kelly tests were compared to identify a trend line between 6 mo and 1 yr in space.
Neuro-Mapping	Quantified neurocognitive changes and associated neural structural alterations occurring as a result of ISS missions by using cutting-edge imaging techniques and a battery of sensory, motor, and cognitive assessments to investigate neuroplastic and maladaptive brain changes. This investigation performed structural and functional magnetic resonance imaging (MRI and fMRI) of the brain to identify the relationship between changes in crewmember neurocognitive function and neural structural alterations following the 1YM. Three data collection sessions were added to this mission.
Fine Motor Skills	Determined the effects of long-duration microgravity and of different gravitational transitions on fine motor performance to enhance future interactions with touch-based technologies, repairing sensitive equipment, and a variety of other tasks. A set of touchscreen tablet-based tasks evaluated the crewmembers' capabilities for controlling and manipulating on-screen icons with precision and reproducibility. This investigation supplemented the two other sensorimotor investigations by providing an additional measure of functional performance postflight and a new sensorimotor functional test in flight.
Hip QCT	Monitored changes in hip bone structure as determinants of fracture risk in response to in-flight bone countermeasures to help define the response of hip bone structure to spaceflight, to countermeasures, and after return to Earth. Pre- and postflight quantitative computer tomography (QCT) monitored the effectiveness of in-flight countermeasures in protecting the integrity of hip subregions that are determinants of fracture risk. 1YM data were compared to prior research (data sharing) on hip bone structure and in-flight countermeasures.
Sprint	Evaluated the efficacy of the Sprint high intensity, low volume exercise prescription to minimize loss of muscle, bone, and cardiovascular function during ISS missions. Pre, in-, and postflight testing and data sharing with selected ongoing medical assessment tests were used to evaluate the effectiveness of this candidate prescription (active group) in comparison with normal in-flight exercise (the control group). Monthly data sessions were extended for the 1-yr mission duration.
Cognition	Through a comprehensive battery of tests, measured how spaceflight-related physical changes, such as microgravity and lack of sleep, can affect cognitive performance. Provided rapid objective assessment of a range of neurocognitive performance functions in spaceflight. Kelly's session dates were altered to match NASA's Twins Study[‡]; Kornienko's sessions were consistent with standard ISS missions (6 mo).
Journals	Reviewed and analyzed astronaut journals, which provide direct insight into behavioral and human issues through the introspective accounts of crewmembers. Performed a systematic content analysis of journal entries via a software program on the Station Support Computers, with a file downlinked to ground systems. This study continued research from two earlier studies, which provided baseline comparisons. Journal entries were submitted on Station Support Computers and weekly data files were downlinked to ground systems.
PVT/RST	Provided immediate feedback to identify objectively when crew performance capability is degraded by various fatigue-related conditions that can occur because of spaceflight through a self-test that measured changes in responses. This investigation continued research from earlier studies and was brought back to augment the dataset for a previously completed experiment. 1YM data were compared to prior Russian Interactions-2 research. Effectively evaluated the extent to which PVT performance was sensitive to factors resulting from the mission environment.
Biochem Profile	Studied biomarkers, or indicators of health, by determining the time course of metabolic changes during and after spaceflight and in relation to other factors (gender, countermeasures, mission duration, dietary intake, and environmental factors). 1YM data were compared to prior research. Three data collection sessions were added to the schedule established in previous study.
Salivary Markers	Determined if spaceflight-induced immune system dysregulation increases infection susceptibility or poses a significant health risk to crewmembers aboard the ISS, and examined the relationship between changes in those biomarkers and changes in other stressors associated with spaceflight (i.e., circadian desynchronization, sleep loss/disruption, mood state disturbances, stress, and infection incidence). 1YM data were compared to prior research. Technical issues led to the loss of more than 50% of the expected questionnaire data over two in-flight sessions; science loss acceptable.
Cardio Ox	Determined the effects of long-duration spaceflight on measures of inflammation and oxidative stress and measures of arterial structure and function; determined how alterations in vascular function and structure correlate with changes in circulating biomarkers of inflammation and oxidative stress; monitored atherosclerotic risk of astronauts for up to 5 yr after the completion of their long-duration spaceflight missions.
Sleep	Examined the effects of spaceflight, ambient light exposure, and crewmember activity on sleep, circadian system, and alertness by evaluating actigraphy, photometry, and sleep logs. 1YM data were compared to prior research. Sleep monitoring occurred three times preflight, almost continuously in flight, and during the first 15 d after landing.
Habitability	Assessed habitability (design and layout) on the space station to determine whether a mission's duration impacts how much space crewmembers need, and informed design of future spacecraft environments for long-duration missions. The study collected human factors and habitability data in flight in near real-time. Analyzed vehicle layout and space utilization, including an analysis of videos to assess translation strategies. One data collection session was missed due to hardware/software issues.
Microbiome	Determined how the composition of the human microbiome may change during long-term space exploration; evaluated potential impact on the immune system and an individual's microbiome. This experiment characterized the prokaryotic and viral microbiome from various body sites at several times before, during, and after the 1YM, along with immune function by analyzing saliva samples for reactivated latent viruses and cortisol levels as well as blood samples for cytokines. Two data collection sessions were added to the schedule established in previous spaceflight investigations.

[‡] Astronaut Scott Kelly and his homozygotic brother, astronaut Mark Kelly, took part in a first-of-its-kind NASA Twins Study, evaluating the effects of spaceflight at the genetic level. The Twins Study introduced 10 integrated investigations. Scott Kelly's participation in the Twins Study overlapped with planned 1YM investigations. While Scott Kelly took part in studies aboard the Space Station, his brother Mark participated on Earth as a ground control subject.

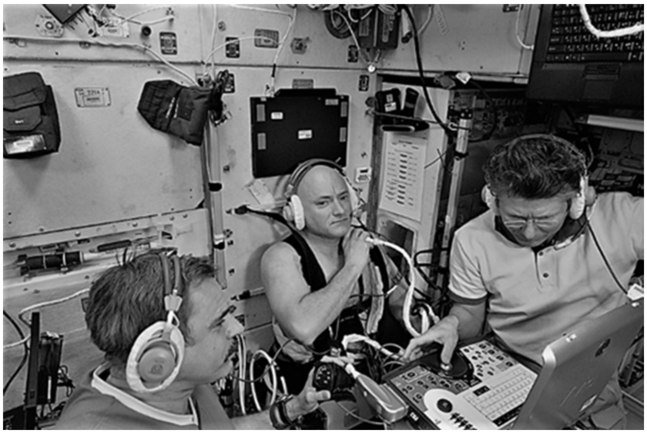

Fig. 3. Scott Kelly as test subject for the Fluid Shifts investigation. Cosmonauts Gennady Padalka and Mikhail Kornienko assist Kelly with the test. Credit: NASA.

to permit extrapolation to early interplanetary expeditions with durations of up to 2 to 3 yr. Therefore, HRP has solicited proposals in the area of analyses of the temporal nature of human adaptation to long-duration low-Earth orbit missions.[1] The selected proposals will populate a multiyear integrated 1-yr mission project (i1YMP) consisting of five 1-yr missions on the ISS (for a total of 10 crewmember subjects), five standard-duration 6-mo ISS missions (10 subjects) paralleling the year-long expeditions, and five short-duration crew vehicle exchange expeditions (10 subjects) lasting up to 2 mo to occur at the approximate midpoint of each year-long expedition. The coordinated nature of the short, standard, and yearlong missions is specifically in support of the extrapolation to multiyear exploration missions. The solicitation does not commit NASA or the other ISS partner agencies to undertake these missions, but it signals the determination of NASA's Human Research Program to be prepared in that eventuality.

A suite of spaceflight standard measures is now in place. This comprises a set of key measurements designed to characterize the effects of space on human health, now taken in a consistent sequence prior to, during, and after all ISS missions, on a voluntary basis. Astronauts participate in standard measures through six laboratory test areas, monitoring their immune systems as well as sleep, cognition, balance, and stress levels.

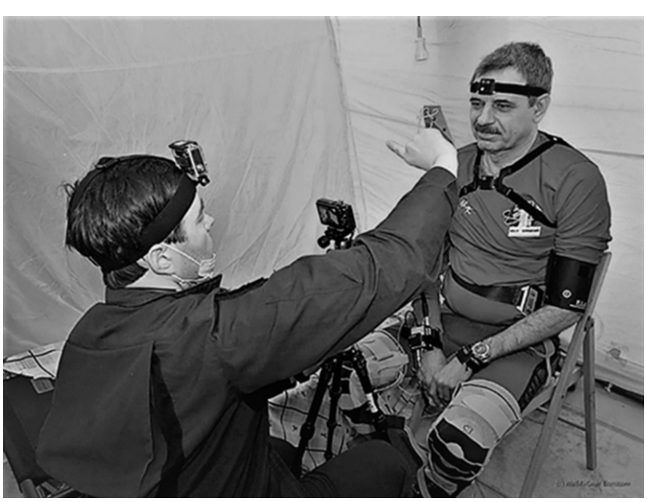

Fig. 4. Kornienko executing a portion of the Field Test shortly after landing in Kazakhstan. Credit: IMBP (Institute for Biomedical Problems). From http://spaceflight101.com/iss-expedition-46/photos-of-mikhail-kornienkos-field-test-after-return-from-a-year-in-space/.

The Kelly-Kornienko 1YM is the first of many steps required for safe and productive human missions to Mars. Results from this mission have provided us with initial findings on the most critical aspect of exposure to spaceflight hazards: time. The programmatic aspects of preparing for and implementing this unique class of mission have established important protocols for astronaut health studies. Experience from the 1YM can be taken as lessons learned to inform experimental design and support future discovery as space agencies make the next giant leap in human exploration of the solar system.

ACKNOWLEDGMENTS

The authors thank the crewmembers for their participation. They would also like to acknowledge the help and expertise of the American and Russian teams who played technical and supporting roles with this work, especially Laurie Abadie, Michael Barratt, Valery Bogomolov, Barbara Corbin, William Gerstenmaier, Peter Hasbrook, Cynthia Haven, Igor Kofman, Charles Lloyd, Jon McFather, Joel Montalbano, Pasha Morshedi, William Paloski, Steven Platts, Katherine Reeves, Julie Robinson, Igor Savelev, Michael Suffredini, and Amanda vonDeak.

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REFERENCES

1. Appendix C. Topics in biological, physiological, and behavioral adaptations to spaceflight: One year mission project and other opportunities. NASA Research Announcement 80JSC017N0001, National Aeronautics and Space Administration (NASA); 2017. [Accessed 2018 April 4]. Available from https://tinyurl.com/HERO-BPBA.
2. Basner M. Individualized real-time neurocognitive assessment toolkit for space flight fatigue. 2017. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11018.
3. Bloomberg J. Physiological factors contributing to postflight changes in functional performance (Functional Task Test). 2015. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10159.
4. Czeisler C. Sleep-wake actigraphy and light exposure during spaceflight. 2017. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11044.
5. Dinges D. Psychomotor vigilance test (PVT) on ISS. 2017. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11278.
6. Dulchavsky S. Microgravity associated compartmental equilibration (MACE). 2013. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=9027.
7. Experiments and researches from 2013: man in space. S.P. Korolev Rocket and Space Corporation (Energia). [Accessed 2018 April 4]. Available from https://www.energia.ru/en/iss/researches/human/all.html.
8. Experiments by expedition. National Aeronautics and Space Administration (NASA). 2015. [Accessed 2018 April 4]. Available from: https://www.nasa.gov/mission_pages/station/research/experiments/experiments_by_expedition.html#4344.

9. Gray G, Johnston S. 3: Medical evaluations and standards. In: Barratt MR, Pool SL, editors. Principles of clinical medicine for space flight. Berlin: Springer; 2008:65.
10. Hargens A. Fluid distribution before, during and after prolonged space flight–NNX13AJ12G. 2017. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11112.
11. Holden K. Effects of long-duration microgravity on fine motor control skills. 2016. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10879.
12. Lorenzi H. Study of the impact of long-term space travel on the astronaut's microbiome. 2017. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11370.
13. Manned transport spacecraft Soyuz S. S.P. Korolev Rocket and Space Corporation (Energia). [Accessed 2018 April 4]. Available from https://www.energia.ru/en/iss/soyuz-ms/soyuz-ms.html.
14. Otto C. Prospective observational study of ocular health in ISS crews. 2016. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10572.
15. Platts S. Defining the relation between biomarkers of oxidative and inflammatory stress and atherosclerosis risk in astronauts during and after long-duration spaceflight. 2016. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10353.
16. Ploutz-Snyder L. Integrated resistance and aerobic training study (Sprint). 2016. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10386.
17. Reschke M. Recovery of functional performance following long duration space flight. 2017. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11413.
18. Seidler R. Spaceflight effects on neurocognitive performance: extent, longevity, and neural bases (NeuroMapping). 2017. [Accessed 2018 Jan. 3]. Available at: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11314.
19. Sibonga J. Feasibility study: QCT modality for risk surveillance of bone - effects of in-flight countermeasures on sub-regions of the hip bone. 2014. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=9924.
20. Simpson R. Effects of long-term exposure to microgravity on salivary markers of innate immunity. 2017. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10947.
21. Smith S. Biochemical profile: homozygous twin control for a 12 month space flight exposure. 2017. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11233.
22. Smith SM. Nutritional status assessment: SMO 016. 2015. [Accessed 2018 Jan. 4]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=9843.
23. Space life & physical sciences research & applications division task book. National Aeronautics and Space Administration (NASA); 2018. [Accessed 2018 April 4]. Available from: https://taskbook.nasaprs.com/Publication/welcome.cfm.
24. Stenger M. Distribution of body fluids during long duration space flight and subsequent effects on intraocular pressure and vision disturbance. 2016. [Accessed 2018 Jan. 3]. Available from: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10871.
25. Stuster J. Behavioral issues associated with long duration space missions: review and analysis of astronaut journals—extension (Journals). 2017. [Accessed 2018 Jan. 3]. Available at: https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=11077.
26. Thaxton S. Vehicle NHV and habitability assessment. 2016. [Accessed 2018 Jan. 4]. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=10878.