History of Spaceflight and the Central Nervous System

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Introduction

Early Discoveries

The concept of human space exploration dates to as early as the Renaissance with famous astronomers such as Nicolaus Copernicus and Galileo Galilei. With the help of the newly discovered telescope, they determined that outer space is an actual place filled with planetary bodies and stars. They questioned the widely believed geocentric dogma of Ptolemy and simultaneously challenged Christian religious ideals about humanities unique and exclusive relationship with God [1]. The visionaries Johannes Kepler and Cyrano de Bergerac conceptualized the idea of space travel and proposed the difficulties that may be encountered with interplanetary flight in the vacuum of space [2]. Science fiction writers of the nineteenth and twentieth centuries like Jules Verne, H.G. Wells, Edward Everett Hale, and Arthur C. Clark were able to incorporate sophisticated scientific principles to space travel and alien encounters making these works ever more exciting and plausible to the general public. Although only fictional tales, their intellectually sound writings about satellites and orbital flight around earth influenced a generation of scientist and engineers who went on to bring these fantasies into reality.

The dearth of research and technological feats over the past few centuries has helped us realize the celestial goals and aspirations of our predecessors. For the most part, each organ system has been extremely resilient to the extraordinary conditions this earth has placed upon them; however, they each function differently in the spaceflight environment. The effects of microgravity, acceleration, vibration, cabin pressure, carbon dioxide concentration, radiation, and extreme temperatures must all now be considered during spaceflight. This book will attempt to provide a comprehensive overview of the known physiologic and biochemical changes that occur in the human central nervous system during short- and long-duration spaceflight.

Early Rocket Science

At the end of the twentieth century, the study of the universe and speculation about the nature of spaceflight were not closely related to the technical developments of rocket aeronautics. This was until 1903 when Russian theorist and schoolteacher Konstantin Tsiolkovsky published his article "Exploration of Cosmic Space by Means of Reaction Devices." In it he laid out many of the principles of modern spaceflight using rocket propulsion. His future publications continued to develop sophisticated aspects of spaceflight including fundamentals of orbital mechanics, space vehicles, and space stations [3]. His pioneering work, though mainly theoretical, influenced modern rocket pursuits and served as the foundation of the Soviet space program.

Robert Goddard from the United States and Hermann Oberth, a German national, elaborated on rocket design, engineering, and propulsion often times in the face of harsh public criticism. Oberth's original doctoral dissertation on rocket-powered flight was rejected by the University of Heidelberg in 1922 for being too speculative. The work explained the mathematical theory of rocketry, applied the theory to rocket design, and discussed the possibility of constructing space stations and traveling to other planets. Goddard went on to patent, construct, and test his ideas on rocket components and liquid propellants.

In the 1930s and 1940s, Germany, Russia, and the United States were on the forefront of rocket development. Rocketry evolved from a theoretical discipline to incorporate large-scale experimentation and practical application. Although the prospect of space exploration was the primary motivation of many early engineers, international conflict and the inevi-

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table weaponization of liquid fueled rockets caught the attention of military organizations. After World War II, the United States and the USSR were political and military competitors in what has become known as the Cold War. Both the countries prioritized the development of orbiting reconnaissance satellites for intelligence acquisition. Concurrently, the public and national governments became more receptive to the idea of sending humans to outer space.

Early Space Exploration

The Soviet Union

The Soviet Union initiated the modern space age with the Sputnik program (1957–1960) beginning with the launch of a low orbit satellite called Sputnik-1. Then, on November 3, 1957, Sputnik-2 carried the first living creature into outer space, a dog named Laika. This marked the beginning of a new era of biological and technological sciences. Soon after, the Vostok program (1961–1963), starting with Vostok 1, carried the first human into outer space, a Soviet cosmonaut named Yuri Gagarin. Gagarin made one orbit around the earth lasting 108 minutes. The original Vostok spacecraft was redesigned by the Soviets to carry as many as three persons and subsequently renamed Voskhod (1964–1965). There were two Voskhod missions, the second of which cosmonaut Aleksey Leonov became the first human to leave an orbiting spacecraft. The Soyuz program (1967–1971) brought about the Soyuz spacecraft which still remains in use to this day.

The United States

The National Aeronautics and Space Administration (NASA) was formed on October 1, 1958, in response to the Soviet Union's launch of Sputnik-1. NASA absorbed the National Advisory Committee for Aeronautics and several other research and military facilities to consolidate the efforts of all future US space exploration. President Dwight Eisenhower tasked the new administration to launch and retrieve a person safely from space. Project Mercury (1958–1963) went on to accomplish this on May 5, 1961, after the successful suborbital spaceflight of Alan Shepard. The Mercury program altogether yielded two 15-minute suborbital fights and four orbital missions of 5, 5, 9, and 34 h.

Soon after, the Gemini program (1961–1966) was designed to demonstrate the feasibility of long-duration space flight. Gemini in total exposed 16 astronauts to 10 orbital flights up to 14 days duration, similar to that of planned lunar missions. These first programs did not identify any medical or physiological problems that could prevent missions of 2 weeks duration or longer.

The Apollo program (1967–1972) was designed with important goals of advancing spaceflight technology, developing human capability to work in the lunar environment and carrying out a scientific endeavor to the Moon. It was the first time significant medical findings were identified in US astronauts including vestibular disturbances, post flight orthostatic intolerance, decreased exercise tolerance, cardiac arrhythmias, and decreased red blood cell mass and plasma volume [4].

The Apollo-Soyuz Test Project (ASTP, 1975) was a joint program between the United States and the Soviet Union with both practical and political agendas. ASTP tested systems for rendezvous and docking should a need for an international space rescue ever be needed. ASTP was followed by the Space Shuttle (or Space Transportation System, STS) program (1981–2011) uniquely using a reusable spacecraft and crew piloted landing. The Space Shuttle changed dynamics of space flight missions. Larger crew sizes enabled flight with pilots, responsible for flying and maintaining the orbiter, mission specialists responsible for experiments and payloads, and payload specialists to tend to specific onboard experiments. The shuttles had standard level atmospheric pressure and gas mixtures and the ability to fly dedicated spacelab modules to conduct scientific investigations in microgravity.

Early Space Stations

The development of a space station was originally an interim step in the US pursuit to land on the Moon. However, in 1961, President John F. Kennedy committed the United States to landing on the Moon before the decade was over, thereby expediting the Apollo program. In the mid to late 1960s, the US Air Force pursed a program called Manned Orbiting Laboratory (MOL) with advanced camera equipment to facilitate military reconnaissance [3]. MOL was canceled the same week as the Apollo 11 moon landing in 1969 was in favor of a NASA project called Skylab. Skylab, therefore, became the first US space station and afforded an opportunity to explore in-flight testing of the physiologic changes of long-term exposure to microgravity. It was also spacious enough for astronauts to freely move around and fully adapt to the spaceflight environment and first to provide a complex set of vestibular experiments [5]. Skylab flights 2, 3, and 4 housed crews in space for 28, 59, and 84 days, respectively (Fig. 1.1).

This show of technological adeptness at the height of the Cold War had several geopolitical underpinnings and raised the question of the military role for piloted spacecraft. The Russians began efforts on a space station in direct competition to the US endeavors. Almaz, the first space station program developed by the Soviets, was similarly intended more for military reconnaissance than for research. For secrecy, it was publicly designated Salyut (1971–1986) upon reaching orbit. Multiple manned missions were sent to Salyut using

Fig. 1.1 This image of Skylab in orbit was taken as the third crew (Skylab-4) departed the space station after 84 days in the orbiting laboratory (https://images.nasa.gov/)

the Soyuz spacecraft as the transport vehicle (Fig. 1.2). This was the first major step in creating a platform for a continued presence of man in space and allowed increasing long stays for crewmembers in outer space.

Salyut went through sophisticated engineering and multiple evolutions to accommodate more crew members. Additional docking ports were added so that long-duration resident crews could receive visitors. Salyut-7 was followed by the Mir space station (1986–2001) after the dissolution of the Soviet Union and the formation of the new Russian Republic. Mir contained a base block derived from the Salyut to function as the crews habitat and was capable of five additional units to carry out scientific pursuits [3]. The establishment of cooperative agreements between Russia and the United States allowed the US astronauts to serve as crewmembers alongside Russian cosmonauts. The NASA-Mir (1994–1995) and Shuttle-Mir (1995–1998) programs paved the way for future cooperation on board the International Space Station (1998–present). Mir was occupied from 1986 to 2000 hosting 100 people from 12 countries (Fig. 1.3).

Fig. 1.2 View of the Soviet Soyuz spacecraft in Earth's orbit, photographed from the American Apollo spacecraft during the joint US–USSR ASTP docking mission in Earth orbit (July 18, 1975) (https://images.nasa.gov/)

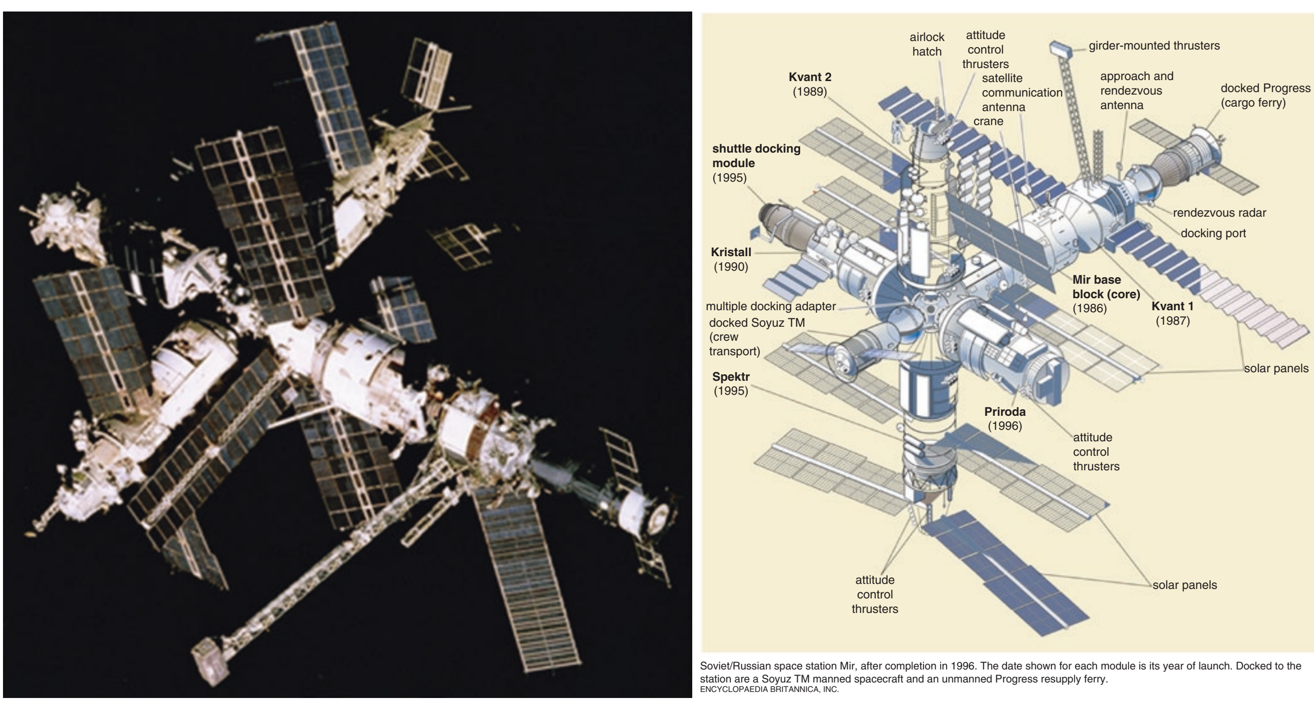

Fig. 1.3 Russian Mir space station photographed approaching space shuttle Atlantis (June 29, 1995) (https://images.nasa.gov/)

International Cooperation

Development of International Organizations

Unlike the United States, the Soviet Union had no publicly acknowledged space agency, instead relying on a variety of state-controlled organizations for conception and development of spacecraft. Rivalry between the various bureaus posed a constant obstacle to a coherent longitudinal vision for the Soviet space program. In 1992, after the dissolution of the USSR, Russia formed the Russian Space Agency to consolidate focus for the country's space policy and programs. It was later restructured and renamed the Russian Aviation and Space Agency in 1999 and then again as the Roscosmos State Corporation for Space Activities in 2004 [6].

In Europe, the French Space Agency (CNES), German Aerospace Center (DLR), the British National Space Center (BNSC), and the Italian Space Agency (ASI) were formed. In 1975, the European Space Agency (ESA) included 15 members—Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Norway, The Netherlands, Portugal, Spain, Sweden, Switzerland, and the United Kingdom. Since 1979, Canada has held the status of cooperating state within the ESA and has become tightly integrated into the institution. The Canadian Space Agency was established in 1990 and maintains a close partnership with many international space agencies.

The China National Space Administration (CNSA) was created in 1993 after the Ministry of Aerospace Industry was split into the CNSA and the China Aerospace Science and Technology Corporation. The former was to be responsible for policy while the latter responsible for execution [7]. In 1998, the CASC was restructured into a number of smaller state-owned companies to be contracted out for operational requirements. China launched its first manned spacecraft in 2003, making it the third country to achieve human spaceflight.

Japan Aerospace Exploration Agency (JAXA) was formed in 2003 with the merger of three formerly independent space and aeronautical science organizations. Since its inception, it has been responsible for the development and launch of satellites and continues efforts toward independent space travel.

The International Space Station

The United States received presidential approval for Space Station Freedom in 1984 and invited US allies to participate in its development. A total of 16 countries and several space agencies came to be involved in the project, making it the largest ever cooperative technological undertaking. The first elements of the station, renamed the International Space Station (ISS), were launched and connected in space in 1998 (Fig. 1.4). Several modules and equipment have subsequently

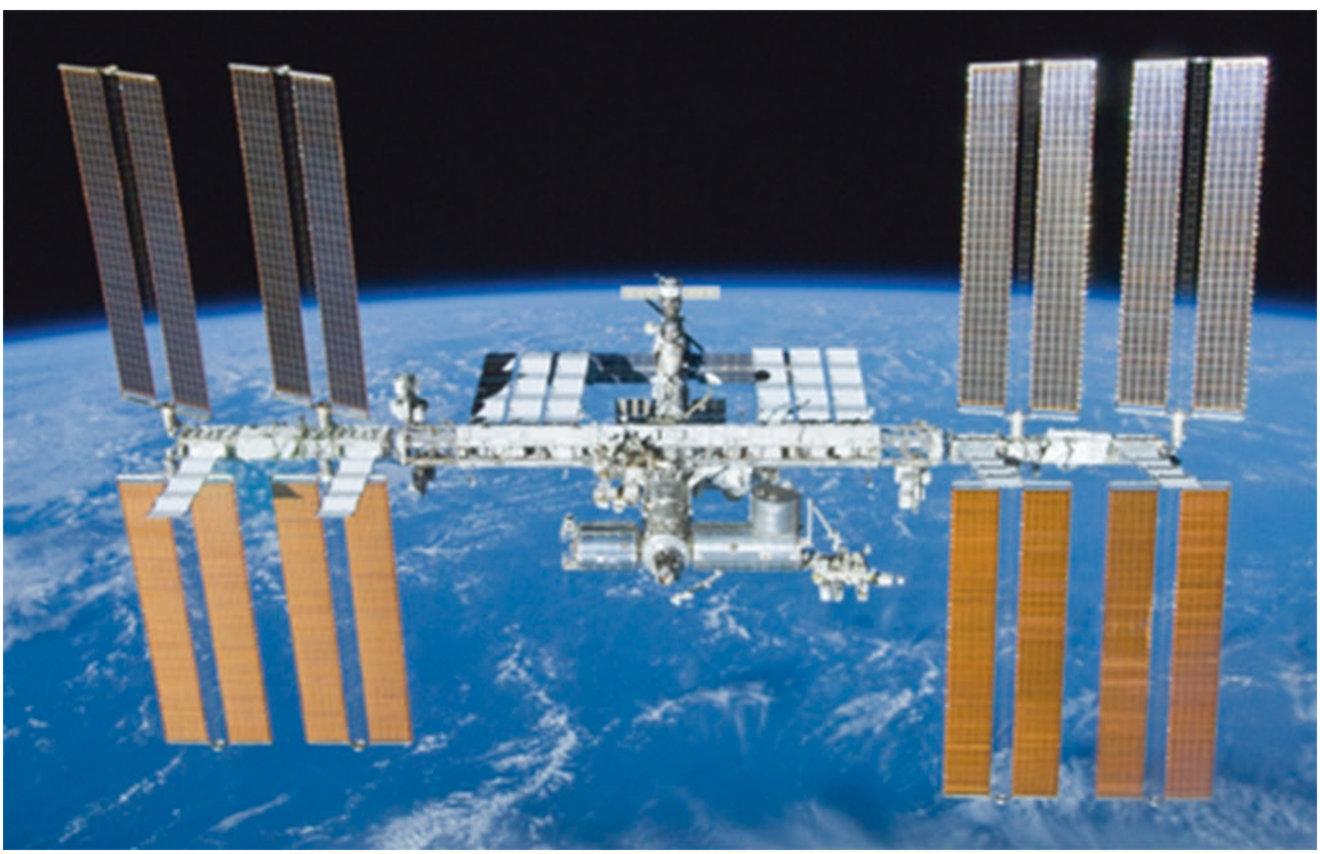

Fig. 1.4 The International Space Stationphotographed by an STS-132 crew member on board the Space Shuttle *Atlantis* after the station and shuttle began their post-undocking relative separation (May 23, 2010) (https://images.nasa.gov/)

been added. The station serves as a microgravity and space environment research laboratory, observatory, and staging base for future spaceflight missions. Since the first inhabitants arrived in 2000, there has been a continuous human presence in space. Much of the early research work by ISS astronauts focused on long-term life-sciences and material-sciences investigations in the weightless environment.

History of Spaceflight Medicine

Human spaceflight has proven to be an exceptionally risky endeavor over the years. Between Soviet and American spacecrafts disasters, 18 people have lost their lives during spaceflight. Human beings have evolved in the Earth's environment, and understanding the effects of low gravity, wide temperature variations, high levels of ionizing radiation, and lack of atmosphere is crucial to safely participating in future long-duration flight.

Aerospace Medicine Organizations

Aerospace medicine was pioneered by Paul Bert of France in the nineteenth century. He has become known as the Father of Aviation Medicine due to his novel research into the effects of air pressure and oxygen toxicity on health. As early as World War I, flight surgeons aided pilots in unique atmospheric conditions and worked closely with design engineers to develop equipment for them to overcome adverse environments. Hubertus Strughold, a former Nazi physician and physiologist, was brought to the United States as part of Operation Paperclip to give the US military advantage over the Soviet Union in the Cold War Space race. Strughold first coined the term "space medicine" in 1948 and was the first and only Professor of Space Medicine at the School of Aviation Medicine at Randolph Brooks US Air Force Base. In 1949, the first Department of Space Medicine was created at Randolph Brooks [8]. The next year, the Aerospace Medicine Association formed the Space Medicine Branch. Soon after, in February 1953, the American Medical Associated authorized the establishment of aviation medicine as a specialty in the field of preventative medicine [6].

Initial Spaceflight Medical Problems

It was anticipated that the first problems astronauts would encounter in spaceflight were those of acceleration and weightlessness. By extrapolating animal experiments utilizing terrestrial rockets, water-immersion, and sensory deprivation, it was thought that the main difficulties would be in the central nervous system and organs of positional awareness. This could lead to disorientation, hallucinations, and psychological adjustment failures in the astronauts. Other immediate problems would be external stresses from noise, toxic hazards in the spacecraft, and ambient space radiations [9].

Physiological disturbance during spaceflight was reported as early as Vostok 2 by the Russian cosmonaut Gherman Titov [10]. Approximately 6 h into the flight, he experienced malaise, nausea, vomiting, and vertigo. This constellation of symptoms was first referred to as "space motion sickness" (SMS) [11] due to the similarity to motion sickness in the terrestrial environment. It is hypothesized that two physiologically distinct mechanisms converge to produce the symptoms of SMS [12, 13]: Cephalad fluid shifts are thought to alter the response properties of vestibular receptors while loss of tilt-related otolith signals in microgravity creates a conflict between the actual and the anticipated signals collected from the external environment. The breadth of symptoms that astronauts report is likely due to a complex interaction between the neurovestibular system and autonomic nervous system [14]. Similarly, the term "space adaptation syndrome" was used when motion sickness was accompanied by head congestion and headaches brought on by a cephalad fluid shift into facial structures [15].

US astronauts would not go on to report these symptoms until Apollo 8 when the crew left their seats during the first orbit to obtain in-flight measurements. It has been suggested that the small confines of the Mercury and Gemini spacecraft limited rapid head and body movement of astronauts within the cabin, thereby decreasing the chances of experiencing SMS during exposure to microgravity [16]. The small number astronauts in the early space program and readily available press access following mission completion made it impossible to anonymize medical data on specific astronauts. This likely prevented astronauts from fully disclosing subjective symptoms and required repeated convincing from flight surgeons that reported difficulties would not preclude them from returning to flight status [17].

Most astronauts require only 2–3 days to acclimate to motion sickness in space and few continue to have residual symptoms during short-term spaceflight [12]. As more time is spent in space, physiologically distinct yet overlapping symptoms seem to arise including headache and visual disturbance. These findings were noted to be similar to the cases of intracranial hypertension in the terrestrial environment which are caused by an elevation in intracranial pressure (ICP) [18].

Spaceflight-induced visual disturbance, first termed by NASA as VIIP, was identified as a serious risk to astronauts during future long-duration space travel, having already affected over 40% of ISS inhabitants [19]. Although VIIP was originally attributed to spaceflight-induced elevated ICP, further factors now seem to contribute. For that reason, it has more recently been referred to as space flight-associated neuro-ocular syndrome [20].

Long-Duration Spaceflight

The first documented neuroscience experiments performed in space were during the third manned mission of the Russian Vostok spacecraft [21]. The vast majority of life sciences experiments on crewmembers have been during short-duration missions, and therefore our knowledge of the effects of long-duration spaceflight is limited. The first 20 missions to the ISS were made up of three crew members living aboard for approximately 6 months. As of 2008, there were only 47 crewmembers with flight durations of 6 months or greater and only four with durations of 1 year or greater. With limited subjects and limited data from the mostly Russian crew, it was difficult to draw adequate conclusions about the effects of long-duration space flight [21]. Since then, the time each astronaut spends in space has dramatically increased. Russian cosmonaut Valery Polyakov spent nearly 438 consecutive days aboard the Mir space station, from January 1994 to March 1995. Cosmonaut Sergei Krikalev has accrued 803 days in outer space in total. Contemporary medicine has now made it easier to measure and track physiologic and genetic changes that occur in the human body. To study these long-term effects better, in 2015 US astronaut Scott Kelly spent 340 consecutive days on the ISS while his twin brother, Mark, remained on the ground.

With time, the cost and risks of human spaceflight have become better able to accommodate the business of space tourism. Although the space shuttle program ended in 2011, private companies such as Boeing and SpaceX have contracts to fly humans to the International Space Station. Other private enterprises with Virgin Galactic and Blue Origin hope to capitalize on a new industry of suborbital space tourism and perhaps help facilitate a permanent moon colony. Unlike the mostly symbolic Cold War moon race, several countries aspire to establish permanent lunar colonies and cultivating and commercializing the moon's yet untapped minerals and resources.

Conclusion

Although there are innumerable harms that face man's spaceflight attempts, little can stop the desire of our species for exploration of the unknown. Little is known as to how the spaceflight environment will alter the anatomical and physiological integrity of our nervous systems and related structures, but aerospace physicians and astronauts should be educated in the current understanding of how human physiology reacts to this extreme environment. It will be critical to develop countermeasures to these known obstacles so that astronauts and civilians can participate at their peak in these missions and return safely to earth. The goal of extending the duration of missions and sending individuals further into space than ever before will challenge the current capabilities of aerospace medicine.

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