Physiological Alterations due to Acceleration and Gravity: A Brief Review of Recent Studies

Name	Affiliation	Contact Details
Shibajyoti Banerjee **(Corresponding Author)**	Saint Petersburg Electro-Technical University ETU LETI (Alumni)	shibajyotibanerjee@gmail.com +91 9330651238
Subarnarupa Banerjee	Kazan State Medical University	subarna.rupa.sr@gmail.com

Abstract

Studies on physiological effects due to gravitation and acceleration have become a hot topic of research since the last century. Scientists and engineers have been putting their best efforts to excavate more about the physiological changes that occur in jet aircraft pilots and astronauts. This study focuses on a few prominent and recent observations related to the alterations of physiological functioning due to gravitational and acceleration forces.

1. Introduction

There is an urgent need for advanced exploration-class countermeasures in spaceflight, although the attempts have been constrained due to the limited availability of data, resources, environments, and proper validation [1]. The primary deconditioning factor during spaceflight is the loss of gravitational loading, and it is imperative to consider the g*r*avity-induced physiological changes occurring in high-stress jet maneuvers or spaceflight.

1.1 History

Artificial gravity is a concept that emerged during the late 19th century when Konstantin Tsiolkovsky realized the inability of the human body to respond well during the free fall in orbital spaceflight [1]. He proposed the concept of rotating space stations, in which centripetal accelerations can provide an inertial loading experience, analogous to terrestrial gravitational loading. On a similar note, Einstein also deemed it impossible to distinguish acceleration from gravitational loading [1]. From 1959 to 1970, insightful studies were pursued on human tolerance under altered gravitational conditions. Since the Skylab program, which pioneered studies on human tolerance to weightlessness for multiple

weeks without prevised thresholds, recent times have further uplifted human abilities to sustain prolonged weightlessness in Low Earth Orbit environment [1].

1.2 What is Artificial Gravity

Artificial gravity (AG) is the simulation of gravitational forces experienced aboard a space vehicle or airplane within the orbit (free fall), or during transit to another planet. An important point to keep in mind is that AG is not gravity at all. To date, the most reliable source for the production of artificial gravity is via centripetal acceleration created through circular motion [1].

1.3 The Mathematics behind G (Gravitational) Forces

From Newton's Second Law of Motion, We know that,

$$F = M \times a \tag{1}$$

Where 'F' is the force in Newton (N), 'M' is the mass of the body in kilograms (kg), and 'a' is the linear acceleration in ms^{-1}. Similarly, the weight of a physical entity can be expressed as:

$$W = M \times g \tag{2}$$

The equations 1 & 2 are analogous, except that the Force component 'F' changes into Weight 'W' which is the force produced due to gravitation acting downwards, and 'g' is the gravitational constant at the surface of the earth, measured as 9.8 meters/second squared. Considering 'n' to be the ratio of 'F' to 'W' gives:

$$\frac{F}{W} = \frac{a}{g} = n \tag{3}$$

Therefore, when a body suffers a force of 'n' G's, the body is acted upon with 'n' times the normal force of gravitation (g) and is perceived as either partial/.hypo (< 1 G), or hyper (> 1 G). Gravitational forces can be further categorized into linear (rectilinear) as in (3), or radial (curvilinear). In simple form, a parabolic flight is mathematically described as [2]:

$$\mathrm{Fcurvilinear} = \frac{MV^2}{R} \tag{4}$$

$$n = \frac{F}{g} = \frac{V^2}{Rg} \tag{5}$$

Where V is the angular or tangential velocity in ms^{-1}, R is the circular radius in meters (m), and n is the ratio of centrifugal acceleration to the gravitational force, expressed as the number of G's, generally in the $\pm$ Gz (head-to-foot) axis. Figure 1 depicts the phases in a typical flight path along with probable G values depicted by the European Space Agency.
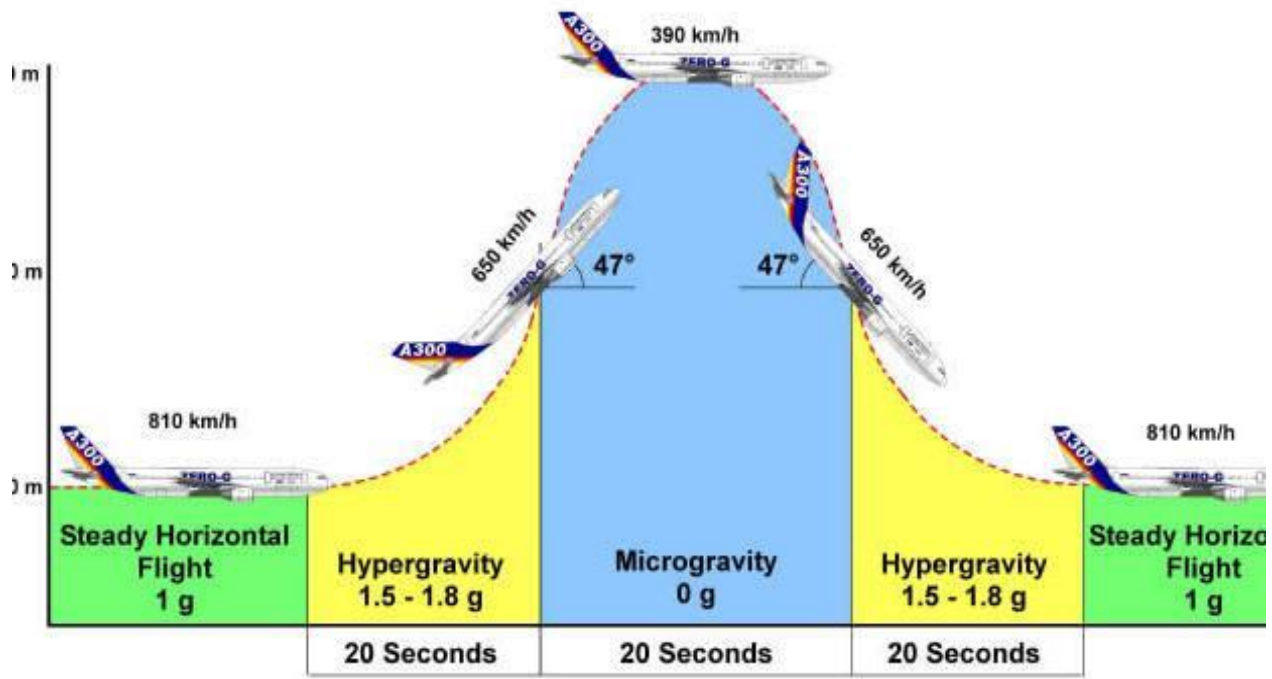
Figure 1: Flight path and Associated Gravity Levels (Image Source: ESA)

2 Physiological Effects of Gravitational (G) forces

Several reports have mentioned physiological problems arising due to altered gravity and Coriolis forces, including changes in oxygenated hemoglobin levels, breathing patterns, Central Nervous System (CNS) lag and delayed stimuli, cardio-vascular activities, immune response, vestibular disorientation, Peripheral Light Loss (PLL) or tunnel-vision, Central Light Loss (Blackouts / Redouts) and Loss of Consciousness, which could prove fatal [2]–[5]. This article focuses on selected studies on different physiological alterations due to micro and hyper-gravity conditions, that are analogous to suborbital space flights and hyper-acceleration experiences, between 2015 and 2021.

2.1 Biochemical Shifts

Biochemical alterations and responses are vital signs of pathophysiological observations induced due to gravity, and studies have been pursued to exemplify these changes. Wochynski and colleagues [6] assessed the fluctuations in lipid indexes as a function of G-stress in centrifuge experiments of cadet pilots and discovered a direct relationship between lipid profiles and their sustainability in centrifuge training [6]. Thiel observed that the adaptation of human T-cells to microgravity starts post two weeks of exposure, and it continues for about six months. Additionally, long-term in-vitro observations are scarce, and minor immunological symptoms that were recorded include sneezing, cold sore, ear pain, congestions, itchiness, pharyngitis, skin infection, rashes, and urinary tract infections arise [7]. Studies led by Tauber experimented with cytoskeleton, metabolism, and cell surface molecules sent

to the ISS for acknowledging the impact of microgravity. The cellular cross-sectional area notably increased post 11 days of exposure, along with a decrease in expression of cell adhesion molecules with the simultaneous release of surface-bound fucose, although no significant changes were observed in the cytoskeletons [8]. Studies on stress responses revealed that spaceflight-induced stresses primarily affect kidneys, bone resorption abilities, muscle loss, immunity, glycaemic control, and endothelial response [9], [10]. Cardiovascular mediating hormones such as galanin and adrenomedullin plasma levels are suggested presyncope markers, and the elevated baselines could be used for analyzing orthostatic intolerance [11]. From neurobiological perspectives, the earth's gravitational pull effectively assists in maintaining the fluctuating states of cells and organelles. Experiments conducted under the Neurolab program reported significant alterations, including reduced expression of genes involved in dopamine synthesis, along with receptor gene expressions in the hypothalamus (i.e. 5 hydroxy-tryptamine 2A or 5-HT2A). Simulated microgravity also induce alterations in the F-actin-cytoskeleton and proteins, cell-membrane lipid bilayers, and electrophysiology of neural ion channels, although there lies adequate scope for further assessment under rotating bioreactors and nervous system development studies [12]. There is a need for assessing cellular morphology on articular cartilages such as chondrocytes that sense and respond to mechanical loading in order to maintain and balance extracellular matrix (ECM) molecule production. Microgravity also affects tumour cell adhesion, migration, viability and proliferation, although the details behind these molecular mechanisms are yet to be uncovered [13], [14]. A small work dedicated to the complexities of cell adherence under microgravity sheds light on the drop in cell adhesion as well as its relationship with tumour growth, metastases and wound healing processes [15].

2.2 Circulatory and Cardiovascular System

Previous efforts by researchers' managed to extract a good deal of information on space flights and military jet maneuvers along with their potential impact on cardiovascular functioning. Progress through recent technology and research has provided the feasibility of studying microcirculatory parameters. There is a dominant fluctuation of parameters under seated postures compared to supine postures, although microcirculation properties remain unchanged in both [16]. Arterial blood pressure and photoplethysmographic alterations are effectively used to assess the impact of microgravity on the vascular system [17] [18]. Similar recorded alterations include cerebral perfusion, G-tolerance, cephalic fluid shifts, decreased central venous pressure, reduced blood plasma volume, loss in red blood cell mass, increased carotid diameter and cardiac output, altered cardiomyocytes, arrhythmias, radiation-induced cardiovascular diseases, and issues due to orthostatic intolerance [19] [20] [21]. The P-wave level significantly fluctuates among military jet pilots, leading to increased serum TSH levels within the body [22]. There have been reports of a decrease in oxygenated hemoglobin, and an

increase in deoxygenated hemoglobin levels at the prefrontal cortex, biceps, and brachial muscles, which could be attributed to hemodynamic changes. Gender-specific studies focused on assessing cardiovascular response under gravitational stresses revealed increased heart rate, along with systemic vascular resistance in women, while the male subjects experienced increased diastolic pressures, indicating a higher orthostatic stability within female volunteers [23]. Further, resting artificial gravity training was more efficient in men and individuals who performed manual exercise, than simulator training or women subjects. There was also a rapid decrease in resting blood pressures in men compared to female subjects [24].

Other miscellaneous yet significant studies related to gravity-induced cardiac physiology include the microgravity tolerance capability in subjects with cardiac-implanted devices during suborbital space flights, and they are assumed to be at risk of arrhythmogenesis, lead displacement, and device damage from gravitational loading and space radiation [25]. Prolonged ectopic ventricular rhythm in response to high G exposure was also reported in a similar study [26], although, the events were short-lived and gradually ceased with deceleration. The assessment of aeromedical factors calls for the development of portable yet resourceful devices, and the finger photoplethysmography is conceived as the most effective method, with the systolic measurement being the most proximal and easiest method of assessing arterial blood pressure levels compared to thermo-dilution, rebreathing, or echocardiography [27]. A review of the electrophysiological experiments in microgravity identifies the influence of gravity on cellular and organ functioning, and there might exist a possible link between microgravity and the functioning of internal ion channels [28].

2.3 Orthopedic Observations and Bone Loss Analysis

Studies on the bone reconfiguration of astronauts and space travelers have been pursued since the discovery of bone loss and counter effects that are induced by microgravity [29] [30]. While Bone Mineral Density (BMD) measurements from dual X-ray absorptiometry remain the conventional method for evaluating skeletal health, it fails to predict fractures accurately. Further, the fracture risk assessment needs consideration of bone material quality and bone turnover measurements [31]. On a generalized analysis, the forearm showed minimal effects to spaceflight exposure, while hips, lumbar spine, femoral neck, and trochanter exhibit greater vulnerability. Areal Bone Mineral Density (aBMD) and volumetric Bone Mineral Density (vBMD) are methods of assessing skeletal health, but these are limited in their capabilities of evaluating fracture risk. Animal experiments show effects such as bone catabolism, bone resorption, diminished biomechanics, growth plate abnormalities, decrease in bone-matrix protein-related genes, and bone formation histology. In parallel, there were shifts in bone architecture from less elongated to more spherical, along with alterations in material properties [32], [33].

Bone loss is the consequence of microgravity-induced impairment of osteocyte and osteoblast functioning, followed by the up-regulation of osteoclast-mediated bone resorption. An average loss of 32.4 % to 36.8 % in BMD is observed during the course of conjunction class missions, while an opposition class trajectory yield better performance with the risk of fracture lying between 15.6 % and 22.0 %, with the diminutions being nonlinear in nature [33]. Experiments were conducted under BION-M1 hardware for accelerated aging and early onset of osteoarthritis, where subjects from Rodent research indicated tendencies of bone loss only [34]. Extended studies on cartilage degradation under microgravity show significant loss of proteoglycan in mice, along with risk factors in astronauts such as degenerative disc disease and arthritis [35], [36]. While the vertical bone, distal tibia, and the femur regain shape post return to earth, the cortical porosity and trabecular bone failed to recover. The distal tibia also succumbed to progressive fragility during post-flight follow-up exams along with spaceflight-induced remodeling imbalance in serum levels of bone resorption markers [37].

Fracture risk during spaceflight remains a grave area of concern, and researchers have meticulously considered the aspects of fracture surgery and healing, along with the comparison and evaluation of bone parameters, fracture risk prediction models, and suggestions for spaceflight induced BMD loss and improved management protocols [38], [39]. Decreased intake of Net Endogenous Acid Production (NEAP) foods and consumption of calcium-rich diet, vegetables and fruits can significantly lower mineral loss under limited manual exercise facilities [40].

2.4 Cerebrovascular Hemodynamics and Oxygenation

Research on hyper- and hypo-gravity-induced changes in cerebral hemodynamics has been progressive. Although the impact of gravity on cerebrovascular flow is more prevalent in fighter jets and extreme maneuvers i.e. hyper-gravity, manned spaceflight, and sub-orbital exploration missions have recorded similar observations. The human body in everyday life is exposed to multiple short hypergravity experiences due to postural changes (0 - 1 G), transient accelerations on roller coasters and Ferris wheel (0 – 4 G), and airplane landing (~ < 1.3 G), directed from the head towards foot ($\pm$ Gz). The cerebral blood flow volume changes as a function of gravitational pull, estimated from 0.5 to 2.0 Gz, although the Mean Arterial Pressure (MAP) tends to remain static [41]. Changes in posture can significantly affect intracranial pressure as well as cerebral auto-regulation, and this calls for further investigations [42]. Linear intensification of G loads assessed from human centrifuge tests in pilots ominously reduces stroke volume, while the heart rate increases to compensate for cardiac output differences [43]. Although it was previously observed that mild hypergravity affects cerebral blood flow, recent studies have been unable to vindicate the reduction of cerebral blood flow under

hypergravity conditions, with experiments being performed at + 1.5 Gz centrifugation [44]. In contrast to the previous study, the authors discovered that the mean cerebral blood flow velocity at the middle cerebral artery and its mean arterial pressure, and the mean arterial pressure of the heart exhibited varied patterns during 21 minutes of 1.5 Gz exposure [45]. In addition, the cerebral blood flow initially decreased before plateauing after a certain interval. While higher values of acceleration lead to greater changes in mean stroke volume, cardiac output, brain oxygenation, and heart rate, it adversely results in a significant decrease in brain frontal lobe oxygenation, along with pooling of blood at the lower extremities and lower parts of the abdomen [46]. A short experiment exhibited the alteration in heart rate with change in body posture, and compared to the change in heart rate using a single sensor, to measure carotid pulse signal as a function of Gz stress in a non-invasive manner [47].

Similar experiments were performed to understand the cerebrovascular physiology under micro-gravity. In the first place, it is essential to understand and observe the changes that occur either during short-term or prolonged exposure to partial gravity. NASA reports that about 40 to 60 % of the crews face neuro-ocular syndromes that could be assessed and comprehended using a planned MRI diagnosis, with dose-response curves and analysis of pre and post-flight statistics that can facilitate the understanding of these syndromes [48]. Contradictions have been existent over the views on accurate ICP (Intra Cranial pressure) measurements in astronauts, and elevated ICP induced abnormalities such as chronic headaches, visual blur, pulsatile tinnitus, and diplopia, which are yet to be documented for spaceflight environments [49]. Although postural changes largely influence ICP in humans, there is a lack of evidence on increased ICP due to zero gravity [50]. There is also an observed upward shifting of the brain, narrowing of the central sulcus, and narrowing of CSF spaces from MRI scans, that can influence visual impairment and ICP, along with ventricular expansion, regional sensorimotor, and cerebellar structural changes [51], [52].

2.5 Neurobiology

Changes in brain functioning are a vital and significant indicator of physiological disturbances imposed due to gravitational variations. In recent times, studies have been simultaneously pursued in the areas of hypergravity and microgravity. Areas of focus on hypergravity-induced conditions include activation of neural cell culture and its influence on the autonomic nervous system, a marked decrease in vestibulo-cardiovascular reflexes, hippocampus plasticity, increased EEG activity, and irregular mono-aminergic innervations of the spinal cord [53]. Manual control performance factors were studied to assess perceptual upright maintenance capabilities in parabolic flight simulators followed by the performance in 1-G and hypergravity (1.5 G). A fall in performance was observed in individuals

with no prior exposure to hypergravity, although continuous exposure reduces adaptation time [54]. Exposure to high acceleration rates significantly increased Brain-Derived neurotrophic Factor (BDNF) and Cathepsin B (CTSB) in test groups and could be attributed to the high strength isometric movements of humans to counter high pressure [55]. There is a decreased intracranial activity at hypo gravity in the Broadmann regions 18 and 39, as observed in miniature aircraft with an achievable acceleration of 0.05 G for about 6 seconds [56]. Hilbert Huang Transform or HHT under conditions of 1-G and hyper-accelerations indicated a rise in amplitude of low-frequency EEG components under 10 Hz baseline, along with consistent bursts of 65 Hz near the occipital region [57]. The brain is also sensitive to changes in gripping forces and adapts itself to varying loads at the fingertips, illustrating that the changes to loading forces are adjusted centrally, and not through the periphery [58].

At present, we have limited knowledge on how exactly microgravity affects the human brain, although past experiments have reported psychological issues, cephalic fluid shifts, neuro-vestibular problems, and cognitive alterations. In addition, due to the neuroplasticity of the sensorimotor system, there is an increase of gray matter tissue in the basal ganglia and white matter in the cerebellum [59], [60]. Commonly used techniques for simulation of microgravity involve dry immersion of subjects in thermo-neural water, head-down bed rest, and simulated parabolic trajectories providing experiences of 0.38 G (Martian surface), and 0.16 G (Lunar surface) missions, although there is limited understanding on the influence of microgravity on the cerebellar, sensorimotor, and vestibular organs [60]. Magnetic Resonance Imaging (MRI) scans of NASA astronauts revealed changes in ventricular volume, and deposition of brain parenchyma at the vertex which leads to decreased postural control, increased complexity of motor task completion, and neuro-ocular syndromes [61], [62], [63]. The subjects also experienced reduced deviations in ventricular volume as compared to those who did not suffer from neuro-ocular syndromes.

2.6 Muscular Biomechanics
The impact of gravity on musculoskeletal parameters requires further understanding, although researchers have tried to assess the governing physiology, and some of the recent trends are considered. Assessment of muscle synergy organization during postural recovery responses under the impact of gravity indicates a possibility of training and rewiring astronaut postural control under varied gravitational conditions [64]. Prolonged exposure to hypergravity can induce changes in cell cytoskeleton and disruptions in cell signaling, cell proliferation, and apoptosis [65]. During aerobatic training in pilots, surface electromyogram showed that a few maneuvers accounted for higher activation of the specific muscle of the upper limbs [66]. A study of the body composition and muscular test of air force candidates showed higher amounts of muscular activities and BMI in

qualifying the gravity acceleration test at 6 G's for 30 seconds, with the knee joint maximum muscle strength being the most significant index [67]. There have been attempts to uncover the relationship between physical fitness as a predictor mechanism for flight-induced musculoskeletal pain, although distinct correlations could not be found through MRI assessments [68]. Sports Medicine Teams or (SMTs) were inducted in the United States defense comprising of certified athletic trainers, with sport medicine physicians and support staffs, to provide rapid access in the event of musculoskeletal injuries, and inherently reduce the overburdening of medical facilities. This in turn relieved the defense budget by almost 10 %. [69]. In a different set of studies, aging pilots were estimated to be prone to spinal problems mainly around the cervical region, amplifying the need for physical fitness, as well as professional and planned coaching for physical training [70]. During parabolic flights, trunk motion reduced to almost half during ascent (hypergravity), while wrist activities did not change. In parallel, underwater immersion simulations showed a decrease in both wrist and trunk activities, the former dropping to a much lower level [71]. A post-flight observation of fighter pilot activity exhibited increased paraspinal muscle composition and cross-sectional areas during the initial five years of service [72].

Musculoskeletal loss under microgravity is an area of concern for astronauts and space travelers. The lower limb skeletal sites are at higher risks of bone loss, with the entire hip showing the highest changes in bone mineral density up to (-) 4.59 %, and near (-) 6 % at the tibial epiphysis, although exercising individuals were projected to be at lower risks [73]. Myometric analysis (the evaluation of muscle and tendon biomechanics) was suggested as an accurate and efficient method of assessing the biomechanical and viscoelastic changes in skeletal muscles under microgravity [74]. Further, myotonometry was used for analyzing robust bed rest effects and training-based postural muscle and myofascial tissues, as well as real-time monitoring of human resting muscle tone during resting conditions [75]. Moderate effects occur due to gravitational loading on muscles post 7-14 days of unloading, and the effects enhance within 35 days post unloading although countermeasure activities are necessary for transit periods between 14 - 28 days and above [76]. Treadmill countermeasures are not completely effective in mitigating osteoporosis, and induction of loaded exercises can enhance the effects of bone-loss countermeasures with increased ground reaction forces [77]. Hypo gravity also reduces trunk admittance and is associated with the reduced response of trunk extensor muscles and concomitant increase in transversus abdomins muscle response, which calls for adaptive countermeasures [78].

2.7 Performance, Injuries, and Physiological Degradation

Aviation accidents and injuries are categorized into human-based, environment-based, or aircraft-based, with human errors contributing to 95 % of the total cases. In the case of general aviation, analysis of crashes based upon human gender follows a similar pattern to motor vehicle accidents, reflecting comparatively higher fatalities in male drivers, although some studies have refuted these claims [79]. Statistical comparison of pilot groups that have faced accidents to those that did not can provide predictive information on accident risks. For example, experienced groups (i.e. higher certifications, number of flying hours, age) are at lower risk compared to newbies [80]. However, the scenario does twist a little in the case of military aviation. The Aircrew Management Programme or ACP, introduced in the Royal Air Force is a structural program aimed to enhance aircrew performance through repeated exposure and adaptation to Anti-G Straining Manoeuvres or AGSM to reduce stain injuries in the neck region, and it showed appreciable outcomes [81]. In the future, the RAF intends to upgrade the ACP program for high +Gz accelerations. Experiments with non-human primates such as macaques highlight aorta injuries and spinal fractures as the most common injury types [82]. An assessment of spinal column in piloting candidates for supersonic flights through MRI revealed up to 72 hernias, 44 bulgings, 66 dehydration of spinal discs, 107 Scmorl nodules, 24 angiomas, and 54 spinal bends. With the frequency of single hernias almost twice that of bulgings [83], studies are unable to demonstrate +Gz exposure as a risk factor for spinal disorders [84]. Side-impact neck injuries are a vital consideration for aircraft safety evaluation and studies have proposed an allowable value of neck injury criteria to a maximum of 5 % moderate injury correlating with body mass and other anthropometric factors, although there is a requirement for re-assessing these critical values [85]. A multi-body dynamics study of head-neck injury damage during ejection was validated using frontal-and rear collision tests, and it showed higher probabilities of head-neck vulnerability while the head leans forward and collides with the headrest [86]. There is a synchronized necessity for musculoskeletal training in student pilots and flight surgeons since these issues actively interfere with the pilot's activities and flying abilities [87]. Other significant records in context with flight injuries and degradations include noise-induced hearing loss observation in about 18.4 % of military pilots, with the prevalence being higher in fixed-wing pilots (~ 42 %) compared to rotary-wing pilots (~ 23%), and fixed-wing pilots with more than 2000 flying hours bearing greater risks [88]. Surprisingly, studies indicate that repeated but low +Gz preconditions exhibits a protective effect on liver injury induced by high +Gz in rats, through decreased oxidative stress, preservation of hepatic energy metabolism, and improved cellular morphology [89]. Heart rate and heart rate variability are considered as standard approaches for the assessment of pilot's mental workload, and there exists thresholds beyond which the subject cannot cope up with task demands, and their performance eventually falls below substandard levels [90]. Further, the thresholds of + Gz induced loss of

consciousness or G-LOC was driven by a maximum brain pressure of ~3.1 kPa, calculated using finite element-based models [91]. Post ejection fatalities are rare in nature, although a recent case involved the death of two fighter pilots due to canopy separation, windblast effect, and a combined impact of G-forces and acceleration [92].

Microgravity-induced physiological degradation is mentioned in several studies. From the data accumulated from the MIR space station and the United States Space Program, it is evident that medical emergencies arise every 2.4 years on average, and requires medical equipment. Astronauts need to return to earth for medical reasons every 5 years, while, catastrophic events rendering an individual unconscious aboard occur every 8-12 years [93]. Astronauts and ground personnel are also prone to different injuries including toxic chemical exposure (fuel, oxidizer, ammonia, inert gas, hydrogen, nitrogen, oxygen, and hydrocarbon fuels), fire, blast, or explosions, deceleration/impact, hypothermia, decompression, and radiation exposure. Additionally, spaceflight induces significant physiological issues such as hypovolemia, anemia, osteopenia, orthostatic intolerance, weakness, fatigue, and neurological problems. Common auto-adaptations that are observed include shifts in fluids and electrolytes, reduced cardiovascular activity, changes in pulmonary physiology, neuro-vestibular changes, musculoskeletal degradation, bone metabolism, hematological, immune system, and pharmacological interventions [93]. Research on spaceflight rehabilitation is anticipated to remain as a problem-driven domain to facilitate the exploration of different research protocols that are analogous to the terrestrial assessment of diseases and/or sports. In this view, multinational space agency collaborations are important for pooling relevant astronaut data [94]. Shoulder injuries are the most common while working with space suits, and spacesuit planar hard upper torso is the most significant predictor variable for injuries. These parameters can be further monitored and modified to enhance astronaut operation capabilities, and decrease health risks [95]. Along with shoulder and spine, there have been observations of muscular atrophy, and hand injuries during pre-flight and post-flight sessions [96], [97].

2.8 Respiratory and Cardio-Pulmonary Responses

Physiological attenuation of the lungs due to exposure to gravitational shifts caused significant problems in both pilots and astronauts. Flight-induced atelectasis was first observed in 1958 using aircraft producing high inertial forces, measured from head to foot axes (+Gz) in pilots. Review studies on the effects of hyperoxia on individual breathing patterns and lung volumes under simulated hypergravity conditions ranging from +3.5 to + 5 G's, followed by ultrasound tomographic analysis indicate successful detection of atelectasis due to hyperoxia and hypergravity compression, although uncertainty exists in determining the precise location of interest [98]–[100]. A recent and interesting

case in this regard was the grounding of the most advanced fifth-generation F-35A aircraft due to issues of oxygen deficiency in pilots at cruise. This could be possibly due to an inbuilt hypoxia condition that was also prevalent in F-22, F/A-18, and T-45 trainers [101]. While the assessment of hypoxic levels in pilots is crucial and complex, attempts have been made to accumulate data regarding the same, including algorithmic modeling for hypoxia training in pilots [102], as well as monitoring, recording, and analysis of breathing behavior [103].

Studies on cardiopulmonary effects due to microgravity were analyzed to observe the pulmonary and metabolic effects. The research focus includes assessment of parameters such as rates of oxygen consumption and carbon dioxide production, respiratory rate, tidal volume, respiratory minute volume, respiratory quotient, respiratory gas exchange ratio, metabolic rate, locomotion efficiency, and physiological cost of transport [104], [105]. Although ergometric exercises in head-up and head-down tilt conditions did not show significant differences in cardiopulmonary parameters between Mars and Earth-like simulations, there exist negligible differences in recordings between the experimental and actual microgravity-based observations [106], [107]. Along with the impacts of decompression, extra-terrestrial dust exposure is a significant health hazard for the lungs and is a matter of concern due to the deposition of unwanted particles [108]. The particulate deposition mostly happens along with the peripheral airspaces, which exacerbates the toxicological effects [109]. Studies have also revealed conceivable relationships between paroxysmal positional vertigo, vestibular dysfunction, osteoporosis, high bone turnover, vitamin-D deficiency in patients with osteoporosis, along with observed hypophagia and hypothermic symptoms in astronauts.

2.9 Otolith and Vestibular Response to Changing Gravity

Exposure to varying levels of gravitational force is sensed by the peripheral vestibular system that directs the information to the neural systems for appropriate feedback response. Initially, this change affects the membrane viscosity which modifies the state of ion-channel flow and further manipulates the resting and action potential thresholds thereby affecting the sensitivity of otolith afferents [110], [111]. Microgravity observably lowers the neural conductance factor, while the body tries to sustain the postural balance during the alteration of gravity vectors. The vestibular system inside the human body consists mainly of two organs, namely the otolith that perceives linear accelerations as well as head tilts, and the semicircular canals that sense radial or angular accelerations [111]–[113]. The relation between tilt perception and manual control has also been closely studied [54], [112], [114], [115], and observations indicate strong correlations between hypergravity and manual control, or response to tilt perception. Researchers also raised questions on the impact of long-duration spaceflight on perception, sensorimotor performance, neurobehavioral assessment, and

countermeasures to G-stress [116], [117]. Additional observations in recent times include impacts of vestibular stimulation on circadian rhythms [118], assessment of visual and spatial abilities [119], neuromotor vertical abilities [120], and cerebral arousal performance during parabolic flights by assessing Critical Flicker Fusion Frequency (CFFF) tests [121]. Diverse studies related to physiological performance in High +Gz load or hypergravity conditions have been reported in combat jet attacking and defensive maneuvers [122], and adaptation to changing +Gz levels [123].

To test the sensitivity of the vestibulo-cardiovascular reflex mechanism in maintaining blood pressure under head-up tilt conditions galvanic vestibular simulation-based studies were done. There was a slight increase in blood pressure levels during the pre-spaceflight period, which slowly diminished within two months post-return [124], along with a drop in blood pressure and degraded vestibular physiology in individuals with dysfunctional vestibular systems [125]. The otolith-mediated vestibular response decreased significantly post-return period and was attributed to the postural stimulation conditions i.e. either static tilt or centrifuge [126]. Sensorimotor degradation exacerbates in space, and more effort is required in maintaining the normal physiological conditions, water immersion-based training protocol being a good match in idealizing suborbital environments [127]. Other interesting topics that could be potentially explored include aspects of space motion sickness [128] and its effects on cognition [129].

2.10 Vision

The impact of high-speed maneuvers and aerobatics can directly influence the human visual system. Advanced research is an efficient method of analyzing the effects due to acceleration. Preliminary studies indicate the exacerbation of visual acuity among cadet pilots exposed to positive acceleration (+Gz), and the results indicate a transient change in visual acuity [130], [131], which sometimes precedes with stereopsis symptoms [127], [131]. Similar studies in this regard include the impact of +Gz acceleration in helicopter pilots, and potentials for visual grey-out due to decreased retinal blood blow at +3 Gz to +4 Gz, and the risk of visual blackout at increased +Gz levels [132]. Other observations include the limitations in color perception and color vision [133], increased intraocular pressure and instantaneous drop in eye-level mean arterial pressures [134], and acceleration-induced nystagmus [135].

Studies on the visual and ocular structure under microgravity assessed intraocular pressure (IOP) [136]–[138], spaceflight induced neuro-ocular syndromes that induce oculo-structural changes [139]–[141], changes in optic-nerve dimensions [142], analysis of Vestibular Ocular Reflex (VOR) during

spaceflight [143], and increased proportion of carbon metabolite content, genetic and biochemical induced ophthalmic modifications due to microgravity exposure [140].

3   Future Prospects

Manned spaceflight takes an ergonomic toll because astronauts are susceptible to space radiation and microgravity-induced physiological and psychological effects. Scientists are considering the prospects of whole brain emulation using artificial intelligence for deep space research, in which the organ will mimic human physiology and adaptation. The accumulated data could be further helpful in digitizing humans via chatbot technology [144]. Heat stress influences orthostatic stability and can impair consciousness due to decreased cerebral perfusion. Peripheral cooling can help in mitigating such problems, and such parameters could be studied as loss of consciousness predictors [145]. Experiments on the feasibility of tissue oxygen monitoring during microgravity traversal showed a minute fall in tissue oxygen levels ($1.1 \pm 0.3\%$) and could be implemented for the detection of tissue hypoxia [146]. Despite having technologies for simulation, research still falls short in assessing abrupt changes in gravitational forces during flight, which inspired scientists to develop the high-performance *Einstein Elevator* at the Hannover Institute of Technology Germany, that can simulate micro, hyper, and hypo gravity (microgravity to + 5 G) with high repetition rates [147]. The impacts of hypergravity require equivalent consideration, and +G phases of Earth –Mars and re-entry to Earth can be simulated (up to ~ 9 G/s), along with firm control over angular velocities and onset rates (3 Gz/s, 4 Gz/s, and 6 Gz/s). Subjects should be able to bear 9 Gz/s for about eight to ten minutes, analogous to lift-off conditions [148]. Similar to the requirement of thermal regulation for astronauts, the thermoregulatory model of cockpit environments was assessed in the SAAB Gripen jets, although there is a shortage of literature due to a lack of experiments [149]. There are ongoing investigations regarding the impact of +Gz acceleration on touchscreen performance in advanced generation jets, with statistics confirming a negative impact on usability, although there was a minute rise in accuracy with increasing G-loads [150].

4   Conclusion

Gravitational forces induce more or less a profound impact on human spaceflight= Owing to the lack of evidential data and real-time monitoring capabilities, the exact physiological effects caused by these forces need further understanding. Although the attempts to uncover these effects have exponentially increased in recent times, additional research can provide a better perception, and will be helpful in future parabolic flight-based physiological assessments.

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