HOW THE SCIENCE AND ENGINEERING OF SPACEFLIGHT CONTRIBUTE TO UNDERSTANDING THE PLASTICITY OF SPINAL CORD INJURY

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ABSTRACT

Space programs support experimental investigations related to the unique environment of space and to the technological developments from many disciplines of both science and engineering that contribute to space studies. Furthermore, interactions between scientists, engineers and administrators, that are necessary for the success of any science mission in space, promote interdiscipline communication, understanding and interests which extend well beyond a specific mission. NASA-catalyzed collaborations have benefited the spinal cord rehabilitation program at UCLA in fundamental science and in the application of expertise and technologies originally developed for the space program. Examples of these benefits include 1) better understanding of the role of load in maintaining healthy muscle and motor function, resulting in a spinal cord injury (SCI) rehabilitation program based on muscle/limb loading; 2) investigation of a potentially novel growth factor affected by disuse and spaceflight which may help regulate muscle mass; 3) development of implantable sensors, electronics and software to monitor and analyze long-term muscle activity in unrestrained subjects; 4) development of hardware to assist therapies applied to SCI patients; and 5) development of computer models to simulate stepping which will be used to investigate the effects of neurological deficits (muscle weakness or inappropriate activation) and to evaluate therapies to correct these deficiencies.

INTRODUCTION

Our laboratories study how the nervous system, particularly the spinal cord, controls movement. We also study how the neuromuscular system adapts to changes in the levels and patterns of use as well as to varying gravitational stimuli. More recently, the interaction of the neuronal and endocrine systems in the regulation of neuromuscular plasticity also has become a topic of acute interest. Each of these areas represent important topics for the study of both spinal cord injury (SCI) and gravitational biology. There also are many common benefits of gravitational biology which can be projected to problems associated with aging and with neural disorders such as SCI, stroke and cerebral palsy. The present paper, however, will focus principally on the interactions of SCI and gravitational biology. The impact of gravitational biology to medicine is of a significant magnitude. For example, each year there are over 10,000 SCI and 500,000 stroke patients that are admitted to hospitals, 75% of whom could benefit from being retrained to walk using some of the physiological principles that have evolved from studies of gravitational loading and locomotion in rats, cats, monkeys and humans[13]. In addition, the recent discovery that prolonged bedrest and spaceflight depress the release of some growth factors has enormous clinical implications to the problems of skeletal muscle atrophy and weakness in any condition when the patient is bedridden.

PHYSIOLOGY OF GRAVITATIONAL LOADING: EVOLVING CONCEPTS

The functional modulation of neuromotor pathways by gravitational loading is not a new discovery. However, the extent to which the neural control of locomotion has evolved so that an ensemble of gravitation-related vectors can be accommodated has not been generally recognized. The role of gravity in defining the recruitment of motor pools has been demonstrated in a number of ground-based and spaceflight experiments. For example, it is known that when an animal stands in a 1G environment many extensor muscles are activated, and that the primary source of extensor torque is derived from motor units with a low threshold for excitation[7,8,42]. These motor units are principally of the slow, fatigue-resistant type. Those muscles having a high proportion of slow motor units are the most active during standing and are often referred to as postural or antigravity muscles[7,85]. Some examples of the short- and long-term modulation of neuromotor physiology by gravitational factors are described.

Effects of Loading on "Gravity" and "Antigravity" Muscles

When a rat is standing, the soleus muscle (an ankle extensor comprised predominantly of slow motor units) is highly active and the tibialis anterior (an ankle flexor comprised predominantly of fast motor units), is

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inactive. When the hindlimbs of the rat are unloaded (i.e. via hindlimb suspension), the soleus becomes inactive upon loss of contact with the floor, whereas the tibialis anterior shows a marked increase in activation[1,70]. These experiments demonstrate that routine loading conditions at 1G serve as an important source of afferent information which selectively modulates excitation and inhibition of motor pools.

Effects of Chronic Unloading on Motor Pool Activation

When this unloaded condition is maintained continuously for days to weeks, activation of the flexor muscle increases over several days and then remains about 3-fold above normal levels for any 24-hr period for up to 4 weeks. The extensor muscles, on the other hand, progress from virtual electrical silence to approximately normal levels within about 2 weeks of chronic unloading[1]. These data show that a chronic and continuous change in the loading conditions results in a gradual change in the responsiveness of motor pools in the absence of loading.

Changes in Motor Pool Activation After Unloading in the Rhesus

Chronic unloading of the Rhesus lower limb as a result of spaceflight is an example of how the relative recruitment of synergistic motor pools can be affected by loading conditions. Upon return to 1G following 2 weeks at 0G, the relative activation of the slow soleus compared to its fast synergist, the medial gastrocnemius, declines, illustrating that the neural strategies that define the levels of recruitment of specific motor pools can be modified by a chronic absence of gravitational loading[43,68]. Similar, but less pronounced, effects are seen after prolonged periods of unloading on Earth[70]. These data suggest that the chronic loading conditions change the relative bias toward excitation of slow vs. fast muscles.

Level of Loading Interpreted by the Spinal Cord

The mechanisms for these modulations in the relative bias of recruitment of multiple motor pools by acute and chronic unloading of the limbs may be mediated by both supraspinal and spinal sensorimotor pathways. The relevance of the spinal pathways has been clearly demonstrated in experiments in SCI subjects with no detectable volitional input to the lumbosacral spinal cord or sensation below the level of the lesion. There is a direct relationship in these subjects between the level of loading on the lower limbs and the level of activation of the motor pools that extend and flex the limbs during stepping[23,39]. Interestingly, similar responses to a range of levels of loading were observed in SCI subjects with some volitional control below the level of the lesion as well as in subjects with the neural axis intact. Similar observations also have been made in the spinal cat[12]. These data indicate that there are spinal cord networks within the lumbosacral spinal cord that are sensitive to the loading conditions in the lower limb that function independently of supraspinal influences.

Temporal Patterns of Motor Pool Activation Modulated by Loading

Loading of the limbs of SCI subjects while on a treadmill provides proprioceptive information other than simply the level of loading[14,15,39]. For example, EMG amplitudes are not only modulated in an appropriate temporal sequence by the level of loading, but the appropriate bilateral sequence of loading of the limbs in an alternating manner provides the afferent information which the spinal cord interprets as load-bearing walking, i.e. the appropriate load patterns and joint actions result in a robust and effective efferent output for stepping. In response to temporally appropriate loading and the associated kinematic and kinetic events of the hip, knee, ankle and toes, the spinal cord generates an efferent pattern appropriate for stepping. Thus, a complex ensemble of afferent information is integrated continuously and in the appropriate sequence for generating stepping. These data indicate that the spinal cord essentially makes complex "decisions" about the afferent state in order to sustain successful stepping[39].

Interpretation and Short-term Memory in the Spinal Cord

The concept noted above is even more dramatically demonstrated when a cat with a complete spinal cord transection is tripped repeatedly during the swing phase of successive step cycles[58]. Upon contact with an object in the trajectory of the foot as it is moved forward, the whole limb is elevated facilitating stepping over the object and continuing uninterrupted stepping. In addition, the subsequent steps are modified as if the cat anticipates the presence of the tripping object. The force of contact with the tripping object is decreased and, in some instances, the cat actually steps over the tripping object without making any contact with it. These motor adjustments reflect complex decision-making within the spinal cord based on afferent information which induces an appropriate motor response to avoid the interruption of the locomotion. Further, the responses to the afferent information are dependent on the phase of the step cycle, i.e. if the same stimulus is presented during the stance phase when the limb is loaded, there is an enhancement of extension rather than flexion. This phenomenon often is referred to as a "reflex reversal"[27]. In addition, the steps following a single or series of tripping events during the swing phase are modified such that the ability to step over the object increases. These studies of Nakada et al.[58] suggest some form of short-term memory in the spinal cord.

Learning In the Spinal Cord

We have conducted a number of experiments in adult, spinal (low thoracic level) cats demonstrating that the lumbosacral spinal cord can be trained to execute stepping or standing[19,20-22,24,44]. Acquisition of the motor task occurs over a few weeks of practicing the particular task for 30 min/day, 5 days/week. The performance of the task improves over ~3 months of training following spinalization. If the task is not practiced, the ability to step or stand declines. These data suggest that a level of "learning" could have occurred in the spinal cord that has not been commonly recognized. The implication of these experiments related to adaptations during spaceflight is that many of the neuromotor dysfunctions observed in the movement control of crew members may reflect newly "learned" motor tasks, i.e. the performance of familiar tasks in some cases, but in a very different gravitational environment. With respect to locomotion, it also seems likely that the efficacy of neuromotor pathways in the spinal cord as well as some of the supraspinal input to these pathways, e.g., the vestibulospinal input, are modified by spaceflight[16,18].

Neural Modulation of Endocrine Function

Results from a series of spaceflight and ground-based experiments have provided clues that proprioception may be a source of modulation of endocrine function[28-30,36,55]. However, it has never been demonstrated that any known circulating hormone is regulated by a known afferent pathway. We now have evidence that muscle proprioceptors, probably muscle spindles and, perhaps, golgi tendon organs, can stimulate the pituitary gland to increase the rate of release of a novel growth factor if low threshold afferents from fast muscles are stimulated. If the same type of afferent stimulation is received from a slow postural muscle such as the soleus, the release of this growth factor is inhibited. These data suggest the presence of a unique link between skeletal muscle afferents and the release of a unique growth factor from the pituitary gland which may play a key role in the atrophic response associated with chronic unloading.

Blunting of Neural Modulation of Endocrine Function After Bedrest and Spaceflight

It was even more striking to find that normal exercise-induced release of this growth factor in humans was completely suppressed by several days of bedrest and returned to a normal response level several days following reambulation[55]. This same phenomenon has been observed in humans exposed to microgravity. For example, in each of four astronauts participating in a 17-day mission, there was a normal increase in growth factor release after 6 minutes of exercise of the ankle extensors before flight. However, following several days of spaceflight, this exercise response was absent. As was the case with the 17 days of bedrest, the response returned to a preflight state within several days after returning to Earth. These data have profound implications for developing countermeasures during periods of chronic unloading[37,38,71,72] as well as for many patients whom are bedridden and experience considerable muscle atrophy.

Myoclonus During Spaceflight

Studies of motor control in the microgravity environment revealed another totally unexpected neurophysiological phenomenon with major implications to motor control in a range of neuromotor disorders, including SCI. We have observed in our Bion Satellite studies that after about 5 days of microgravity, a trained task to push with the foot on a lever results in clonic-like contractions in the Rhesus musculature[68]. These data suggest that clonus, as occurs in a wide variety of neuromotor pathologies such as stroke, cerebral palsy, SCI, brain injury and Parkinson's disease, may have as a contributing factor an unusual pattern or level of use suggesting that some anatomically-defined pathology, such as disruption of supraspinal neural pathways, may not be the only contributing factor. These data also suggest that microgravity may not only modulate the relative recruitment bias of one motor pool compared to another, but it may also result in the loss of some fundamental neurophysiological mechanisms which normally desynchronize the action potentials among a population of motoneurons.

Changes in Myosin Phenotype with Chronic Unloading

Comparisons of the adaptations of skeletal muscle in response to spaceflight and SCI also is of interest because qualitatively similar changes occur in the myosin phenotype, fiber size and mechanical properties[9,10,17,25,35,47,54,63,64,73,76,79,80,89]. In humans and rats, there is a significant increase in the expression of fast relative to slow myosins following spaceflight or SCI and a similar effect seems to occur in the Rhesus following spaceflight. The similarities in changes in muscle fiber properties provide clear evidence that the observed changes are not attributable to some neural pathology, but reflect changes in function of the normal neuromotor system under these chronically unloaded conditions.

Metabolic Effects of Spaceflight on Dorsal Root Ganglion Neurons

Another indication of the extent to which the altered function of the neuromotor system as a result of spaceflight can affect its properties is shown by a decrease in the succinate dehydrogenase activity, an oxidative marker enzyme, in a selected population of rat sensory neurons that have sensory receptors in the limbs[45]. The significance of this finding is that only altered use patterns and levels can change the dorsal root ganglion neurons. It has been assumed almost from the beginning of space exploration that chronic changes in proprioception would be caused by microgravity[62] and this could change the properties of those neurons that provide information about the kinetic and kinematic properties of movements in space and upon return to Earth.

Loss of Myonuclei During Muscle Atrophy Following SCI, Spaceflight and Hindlimb Suspension

It is now clear that when a skeletal muscle fiber atrophies there is a loss of some myonuclei[2-5,11]. Further, we have some evidence that the loss of at least some of the myonuclei during chronic unloading by hindlimb suspension is due to apoptosis. We also have some preliminary evidence from biopsies of astronauts after an 11-day spaceflight that myonuclei are lost after about only 10-15% muscle atrophy. We also studied the modulation of myonuclei number when muscles were hypertrophied by chronic overload[57]. In both cats and rats, the number of myonuclei per fiber increased about 3-fold. There was about a 30% decline in the number of myonuclei when atrophy was induced by SCI in humans. These studies suggest that the volume of cytoplasm sustained in a muscle fiber by an average myonucleus is closely associated with the chronic loading pattern on the muscle. Further, these results suggest that if the loss of myonuclei could be prevented, then the severity of the muscle atrophy could be reduced. This combination of experiments on SCI, spaceflight and hindlimb suspension are consistent with the conclusion that the load imposed on the muscle may modulate protein metabolism, and thus muscle fiber size, by modulating myonuclei number.

METHODOLOGICAL AND TECHNOLOGICAL ADVANCES; SPACEFLIGHT AND SCI INTERACTIONS ACCOMPLISHED TO DATE

Tendon Force Transducer - EMG Implant and Telemetry

We have worked with the NASA Ames Research Center to develop the capability to record in Rhesus 1) forces generated by a single muscle (the medial gastrocnemius); 2) activation patterns (EMG) from four leg (soleus, medial gastrocnemius, tibialis anterior and vastus lateralis) and two arm (biceps and triceps) muscles; and 3) the work output of the ankle muscles, during normal cage activity, performance of a complex foot motor task and running on a treadmill bipedally and quadrupedally (Fig. 1)[43,68]. Also, work output measures are derived from an ergometer built by the Russians, 3-D video analyses of movements and force data from the tendon force transducer. The highly successful execution of this experiment on Bion 11 represents a major achievement in whole body, in vivo integrated physiology for nonhuman primates or any other animal. Unfortunately, NASA chose to terminate the Rhesus Bion Biosatellite Program even though the Program had achieved a significant level of success both technically and scientifically. But be that as it may, the significance of these achievements is that they represent a highly valuable technology that we are beginning to use immediately in studies of SCI and growth factors in other animals. This technological development by NASA occurred over a 7-year period and has provided an experimental model that is immediately ready to be used for crucial studies on how growth factors affect neuromotor in vivo function in a primate.

Figure 1. Telemetered EMG and muscle force signals from a Rhesus monkey walking quadrupedally on a motor driven treadmill at 3 mph. MG, medial gastrocnemius EMG; MG TFT, medial gastrocnemius tendon force transducer; TA, tibialis anterior EMG; Sol, soleus EMG; Tri Brach, triceps bracii EMG; Bi Brach, biceps brachii EMG. MG and Sol are plantarflexors at the ankle, TA is an ankle dorsiflexor, Bi Brach is an elbow flexor and Tri Brach is an elbow extensor.

We are continuing this approach by adapting some aspects of this technology to studying the rat. The individual components of this important technological advance include the following:

1. Development of implantable force and strain devices and electrodes that can remain functional for more than one year;
2. Development of the physiological and medical care procedures to maintain implants in nonhuman primates for more than one year;
3. Development, based on technology developed for space life sciences research, of a commercial telemetry system to transmit forces and EMG signals

synchronized with video tape on limb movements during unencumbered locomotion;
4. Development of a well-defined motor task for an isolated muscle group using psychomotor training programs so that detailed, programmed motor performance can be tested;
5. Integration of neuromotor physiological data with a newly developed Psychomotor Test System (PTS) by Rumbaugh and colleagues at Georgia State University for assessing learning and other psychological parameters;
6. Development of technology to acquire and store extremely large data sets of multi-channel long-term recordings of telemetered data from rats, cats and humans;
7. Development of software to analyze extremely large databases of 24-hour EMG-force recordings;
8. Development of an external calibration device from which muscle mechanical properties can be determined in vivo; and
9. Development of software to assess the relative activation patterns of different motor pools, providing the capacity to define what might appear to be subtle changes in neural activation strategies, while actually representing a significant kind of neuroplasticity that would otherwise be difficult to detect.

Development of Muscle Biopsy Methodology for the Rhesus

Although muscle biopsies have become routine in humans, the procedure differs in the Rhesus because the muscles are smaller and, therefore, the biopsy needle must be smaller. The location of the biopsies also have to be limited because of the need to take multiple biopsies, e.g., before and after spaceflight and after recovery from flight. The need for multiple biopsies required that the muscle sites for each sample consist of different fibers so that repeated samples would not include fibers that had already been cut during a previous biopsy. To avoid this problem, a careful analysis of the muscle fiber architecture was studied and described in a number of hindlimb muscles[66]. Thus, the Rhesus biopsy methodology has been sufficiently developed[6] to use in intervention type of experiments as described above using growth factors and engineered fibroblasts in rats[83] to facilitate recovery from SCI.

Image Processing System

In the early to late 1980's, we worked closely with the Jet Propulsion Laboratory (JPL) to develop an image analysis system, taking advantage of the extensive software that they had developed for their visualization techniques used in outer space probes. With this expertise we were able to build a state-of-the-art imaging system that was about 15 years ahead of the field. This image processing development occurred as part of a Program Project Grant from NIH to study SCI. We have published numerous papers using the single cell enzyme activity and morphological measures based on this technology using several experimental models to include SCI, spaceflight and hindlimb suspension, recovery from these models of unloading and the interaction of exercise and growth factors in response to these models[31,32,40,41,46,48-53,56,59,61,65,77,78,84].

Cuban Boot

An ingenious idea emanating from the Russian Space Program and colleagues in Cuba was that adaptation to the absence of load via the sole of the foot was difficult to achieve during prolonged spaceflight because the ensemble of afferent input to the central nervous system was so incongruent with the normal physiology in a 1G environment. To test this idea, a boot was developed which could be inflated to apply pressure on the sole of the foot and simulate some level of gravitational loading. The technology developed to study this phenomenon is now in the advanced planning stages for studies using SCI patients. We are collaborating with Charles Layne and colleagues at KRUG Life Sciences, Houston, TX and the Johnson Space Center in using an updated model of the "Cuban Boot" to study the role of pressure on the sole of the foot of SCI subjects in generating stepping. This device will help us in differentiating the overall effects of loading and the kinematics of the lower limbs during stepping on the activation patterns of the lower limb motor pools from the effects attributable only to the pressure on the sole of the foot. This device, therefore, can be used to functionally dissect the source and kind of afferent input that the spinal cord of SCI patients can interpret to generate and/or enhance weight-bearing stepping.

TECHNICAL ACCOMPLISHMENTS IN PROGRESS

We are continuing efforts to leverage NASA technology and expertise in our research projects related to SCI. Several areas hold considerable promise in this respect.

Limb Assisting Device (LAD)

We have been developing rehabilitative strategies to improve the locomotor capability of SCI subjects. This technique consists of the subject stepping on a treadmill while being supported by a harness attached to an overhead lift, thus permitting different levels of body weight support. In most of our studies, the subjects are unable to step overground or on the treadmill unassisted, at least initially in the rehabilitation program. Most of these subjects are classified as ASIA A, i.e. have a "complete" spinal injury at the mid- to low-thoracic level, i.e. no detectable sensation or volitional activity below the level of the lesion. To assist the subjects in stepping, therapist aids hold each leg distal to the patella to assist with knee extension during stance and distal to the ankle to assist with swing and foot placement as necessary. As the subject's ability to step improves, she (he) needs less assistance from the therapist aids. A decrease in the level of assistance reflects an improvement in neuromotor function. However, we were unable to quantify the level of assistance provided to the subjects. To solve this problem, colleagues at JPL have designed devices which record in 3-D the forces imposed on the legs by the therapist aids. Thus, as the neuromotor output of the subjects improves as a result of some post-trauma intervention, the forces imposed on the foot and knee will change accordingly (Fig. 2).

Figure 2. Quantification of assistance provided to an SCI subject stepping. The inset shows the location of the measuring devices and the vectors measured by them. (A) depicts assistive forces early in a training session when the subject required assistance throughout the step cycle and (B) when the subject was capable of performing the swing phase of the step cycle with minimal assistance. Shaded regions represent the stance phase and unshaded regions represent the swing phase of the step cycle.

Real and Virtual Stepping of SCI Subjects

Modeling of lower limb stepping is providing new insights in efforts to develop effective rehabilitation strategies to improve mobility in SCI subjects. At the present, we are using a neural network that functions as a central pattern generator[34] with a sensory feedback system combined with closely simulated limb mass, kinetics and moment arm data of individual muscles of the hip, knee and ankle. We also are currently modeling locomotion with the subject walking over a range of relative loads, i.e. fully weight bearing to stepping with no load (air stepping). Variables that are being studied, besides percent of body weight loading, include the speed of stepping, the frequency of stepping and the changes in muscle output, e.g., as would occur with muscle hypertrophy or atrophy.

Intramuscular and Intra-tendon Measures of Stress and Strain in Humans

In vivo measurements of localized stresses and strains within and among muscle fascicles are unknown. In collaboration with JPL scientists and engineers, we are currently developing devices that can measure microstresses and microstrains within and on muscles and tendons of humans. Miniaturization techniques central to current space exploration efforts have made it possible to produce an array of sensors each ~1.0 x 1.0 x 0.1 mm appropriate for surgical implantation. These tiny sensors consisting of a resonant beam transducer and fiber optic linkage will be powered by muscle-generated kinetic or thermal energy supplied by the test subject. Infrared data transmission will obviate the necessity for through-skin leads, eliminating a major source of risk and discomfort. The data generated will be used to refine a computer simulation of human locomotion currently under development (see below) and enhance current models of muscle-tendon function.

This technology is important because the present models of muscle-tendon function are far too simple in that they do not provide accurate estimates of the actual output of the whole muscle-tendon complex during normal movements. The present models fall short because the forces that are generated by sarcomeres along the length of the muscle fibers must be transmitted, in large part, across the membranes and to the interfiber matrix to reach the tendons of insertion and/or origin[26,60,67,81,82]. We have hypothesized that if the actual intramuscular and intra-tendon stress-strain properties were known, we would have a more accurate understanding of the kinetics of the muscle-tendon complex in vivo. Present estimations based on existing models of skeletal muscle sarcomeres fall far short of the actual in vivo output properties of the muscles[33,86].

Exoskeleton of the Human Lower Limbs

As noted above, in conjunction with JPL scientists and engineers, we are studying the ability of the human lumbosacral spinal cord to generate full weight-bearing stepping independent of any supraspinal control. To perform these experiments, we presently assist the movements of the limbs as described above, i.e. with therapist aids manually assisting each leg during the step cycles. This assistance is needed for all "complete" spinal subjects and initially in the training stage for subjects with limited supraspinal connectivity. This approach has two inherent and severe limitations. First, it requires considerable human resources which can only be provided to relatively few subjects. Second, the movements of the limbs only generally approximate the normal kinematics of the human legs during stepping. Thus, an exoskeleton which can manipulate the entire leg in a normal kinematic pattern at a range of speeds would provide a much higher quality of motor training. In addition, such a system would allow us to study more precisely and thoroughly a larger number of subjects and to reach a higher level of success in the level of recovery than can be attained using the assistance provided by humans.

JPL has implemented a prototype robotic exoskeleton for testing on the lower extremities within the UCLA Neurological Rehabilitation and Research Unit. Preliminary data collection from human testing has already proven to be quite encouraging. Completion of the system is pending NIH grant approval. This work has been a joint collaboration between JPL, UCLA, Cedaron Medical Inc. and ATI Industrial Automation, Inc. When completed, this exoskeleton could be used to supplement the torques developed by the patients during locomotor retraining after stroke or SCI. This same exoskeleton could be used to increase the torques required when walking or exercising in space thus helping to maintain muscle mass and bone calcium. This will be accomplished for both SCI and stroke patients through the modeling of locomotion along with the appropriate feedback signals developed from model predictions and input from the exoskeleton.

Cybersuit

In preparation for the Space Station, futuristic devices are being developed to enable scientists to study the kinetics and kinematics of movement in space. We are testing technologies in our Functional Assessment Laboratory with the plan to use them when they become available to the scientific community for studying locomotor performance and arm movements. An easily obtainable means of recording limb motion, as is being planned for the cybersuit, will represent a major enhancement in our ability to assess the effects of training on the locomotor ability of SCI subjects as well as for stroke victims and subjects with cerebral palsy. This suit is being designed to measure a limb segment position in 3-D space using a combination of multidimensional sensors imbedded within a body glove type of suit.

Intrasole Forces

An improved technology in recording forces (pressures) imposed on the sole of the foot during locomotion at 1G and at varying levels of loading represents important and crucial data in attempting to understand the mechanisms of neural control of stepping in control and SCI subjects. As noted earlier, the human spinal cord is highly responsive to the levels and patterns of loading of the legs. The intrasole forces are also important in understanding why bones demineralize in space and in SCI subjects. The impact of forces transmitted through the bones of the foot are thought to be critical biological signals for maintaining bone homeostasis. Measurement and study of similar forces are also likely to help understand how muscle loading modulates muscle protein homeostasis[12a,12b,69,87,88]. Commercially available technology for recording foot pressure is being improved to incorporate in Space Station modules. This will certainly be useful in studies of loading in SCI subjects.

Modeling locomotion

A detailed mathematical model of human locomotion would provide us with a research and therapeutic tool capable of 1) simulating both normal and impaired locomotor strategies; 2) calculating the force levels necessary at each joint to effect successful locomotion; 3) pinpointing, for complete SCI subjects, which weak components of the step cycle need augmentation, and by how much; and 4) devising and assessing alternative locomotor strategies that place fewer and/or less stressful demands on muscle force output. The first steps toward such a model have been taken by Taga's group[74,75]. In a collaboration between the UCLA Brain Research Institute, Mechanical Dynamicss Inc. of Ann Arbor MI. and JPL, we are devising the more advanced locomotion simulation needed to analyze and predict human motion. The simulation is data-driven at present and implements only a single lower extremity with only the minimal muscle groups sufficient for locomotion. However, it incorporates classical Newtonian mechanics with six degrees of freedom, is completely dynamic, and possesses a full graphics interface. It is being expanded to include all necessary joints (hip, knee, ankle and foot) of the lower limbs operating in 3-D space with a neural control module capable of serving as a general purpose test bed for a variety of competing locomotion control models.

The model currently permits us to evaluate the alteration in kinematic, kinetic and ground reaction force dissipation signatures for the lower extremity during walking gait simulations at varying gravity loads. As anticipated, all three signatures from the model predict decreased reliance on the shock dissipation mechanism of the lower extremity under decreasing gravity loads. The model is sufficiently detailed to permit analysis of the passive (heel strike) and active (mid- and forefoot impact) peaks in the ground-reaction dissipation signature to predict effective shock at each joint. In the coming months, addition of a modular neural control model will make possible the testing of a variety of locomotor regulation systems and enable us to make concrete predictions of the force levels and timing necessary for successful locomotion.

SUMMARY

We have briefly outlined a number of examples of where NASA resources have facilitated both technically and conceptually our understanding of how the nervous system, and more specifically, the lumbosacral spinal cord, controls locomotion in humans. It is also true that our efforts to understand the unique aspects of movement control in space and how our neuromuscular system adapts to chronic microgravity environments have greatly benefited from our NIH-related resources. These synergistic interactions continue to occur on a routine and almost daily basis and, in fact, continue to proliferate and become more significant. These interactions permeate our educational and research efforts with students, including high school students via outreach programs, undergraduates, masters and doctoral students, postdoctoral fellows, research scientists and visiting scientists. From an educational perspective, JPL, and the Brain Research Institute and the School of Engineering at UCLA are developing a Neuroengineering Graduate Training Program with a major focus on SCI, stroke and Parkinson's disease as well as emphasizing basic neurobiological processes. In the next generation of scientists, a broader range of expertise in technologies and biological sciences are going to be expected and required to serve the industrial and academic needs in the sciences and engineering. The space biology research program can provide an important training ground for this type of education and experience. Presently, however, the potential contribution of the space biology research program to education and research in the life sciences seems to be tenuous. There is not sufficient evidence of a strong commitment to the life science community that will be necessary to train, sustain and challenge a critical mass of new scientists with an interest in the biology of space. Furthermore, in the absence of this commitment, scientists with an interest in highly integrative physiological systems will not be able to capitalize on NASA's unique combination of scientific and technical resources as we have over the last 15 years. A cooperative effort between NIH and NASA must play an important role in maintaining this critical body of integrative physiologists who will be crucial in the planning and the actual exploration of the effects of spaceflight on humans and other organisms as well as for studies involving neural dysfunction of humans on Earth.

From our perspective, integration of data from International Space Programs (e.g., Bion Program) into our research program has already provided important insights toward understanding the mechanisms of learning motor tasks, the plasticity of the neuromuscular system, as well as how the gravitational environment can shape evolutionary biology. From a clinical perspective, the space biology programs have greatly facilitated efforts to understand and develop more efficacious rehabilitative strategies for those who suffer from SCI, stroke, cerebral palsy and aging. In our opinion, both the value and magnitude of this contribution are consistently undervalued and often are not even recognized. This paper only notes a few examples of the potential of these interactions related principally to one laboratory and its collaborators.

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