Neuroplasticity as a Foundation for Human Enhancements in Space

Margaret Boone Rappaporta\textsuperscript{a}, Konrad Szocik\textsuperscript{b}, Christopher Corbally\textsuperscript{a,c}

\textsuperscript{a} The Human Sentience Project, LLC, 400 E. Deer's Rest Place Tucson, AZ, 85704, USA
\textsuperscript{b} Department of Social Sciences, University of Information Technology and Management in Rzeszow, Sucharskiego 2 Street, 35-225, Rzeszów, Poland
\textsuperscript{c} Vatican Observatory Research Group, Department of Astronomy, University of Arizona, Tucson, AZ 85721, USA

Abstract: The space medicine literature reports changes in neurological systems of astronauts after spaceflight, which has caused understandable concern. Rehabilitative medicine provides a preliminary context to address these changes and creative efforts in preflight training and post-flight remediation have resulted. Research can now begin to determine the neurological changes that are most and least debilitating, the most and least reversible, and which can be tolerated as an adaptation to space. It is not yet known which changes will require remediation with the help of human enhancements, or the type (genetic, pharmacological, prosthetic) when crew venture on long voyages to Mars, the asteroids, and outer planets. Absent from the discussion to date is the biological basis for neuroplastic changes in spaceflight—genetic, developmental, and evolutionary—especially insights from genomics experts and paleobiologists that suggest advantages. Humans are flexible, adaptive, and in many ways, well suited for space with the help of enhancements. Their neurological plasticity provides an almost unique foundation in the animal kingdom for genetic engineering, medication management, and remediation, so enhancements can be integrated naturally into human bodies, lives, and work. Here, the authors explore the nature of human neuroplasticity as a foundation for use of human enhancements.

Keywords: Neuroscience, Human enhancement, Genetics, Developmental biology, Program evaluation, Risk-benefit, Cost-benefit, Space policy.

1. Introduction: Neuroplasticity and Human Enhancements

The space medicine literature reports changes in neurological systems of astronauts after spaceflight, which has caused understandable concern. Rehabilitative medicine provides a preliminary context to address these changes and creative efforts in pre-flight training and post-flight remediation have resulted (Figure 1). Research on post-spaceflight neurology to date
provides the outlines of findings yet to come. Changes in the human brain, sensory apparatus of the inner ear, balance, and locomotion all suggest future challenges [1], [2], [3]. Research must now turn toward defining the neurological changes that are most and least debilitating, the most and least reversible, and which can be tolerated as an adaptation to space [1], [4]. Furthermore, it is not yet known which changes will require remediation with the help of human enhancements or the type (genetic, pharmacological, prosthetic), when crew venture on long space voyages to Mars, the asteroids, and outer planets.

Human enhancements for spaceflight can creatively draw on a wide range of scientific disciplines and technologies (Figure 1), as well as a constellation of social movements and philosophies, while the search accelerates for methods to prepare humans for space and ensure their functioning when they reach their destinations. Even the Moon’s one-sixth gravity may
require remediation, large or small. In response to functional deficits, human enhancements will create an array of changes to the human body, cognition, and consciousness. Therefore, it will be useful to approach human enhancements as a coherent collection of alterations that can be evaluated along common scales, using common metrics, but sometimes different space mission goals.

Understanding the biological nature of neurological changes will allow researchers to ask finely targeted questions, identify which neurological deficits should have priority, and select which deficits are so troublesome, they should be considered for remediation with human enhancements. Government-funded space programs for scientific research and discovery will increasingly join commercial endeavors for settlement and profit, in a search for enhancements that can help humans function in hostile environments. Both governments and businesses will address the remediation of deficits over very long periods of time, in order to accomplish space mission goals. Until artificial gravity is well developed sometime in the future, the focus appears rightly to be on the effects of microgravity.

We present two major themes in human spaceflight research today, with the goal of encouraging a consideration of their interaction: (1) genetically based human neuroplasticity, which occurs at higher levels compared to other mammals, and (2) the emerging array of human enhancements, now deemed “artificial” but in the future, perhaps increasingly “natural” [5].

Humans are flexible, adaptive, and in many ways, well suited for space, with the help of human enhancements. Their neurological plasticity, especially, provides a virtually unique foundation (in the animal kingdom) for genetic engineering, medication management, and neurological remediation, so that enhancements can be integrated naturally into human bodies, lives, and work in space. Humans appear to be able to incorporate enhancements, just as they
incorporated toolkits into the functioning of their hands and minds. No other animal species has
done this to the extent of humans. No other species can do this, until and if artificial intelligences
take over space exploration for us.

2. Evaluation of Human Enhancements

2.1 Importance of Human Neuroplasticity in Spaceflight

Human flexibility, adaptability, and variability in phenotypic expression provides an important
foundation for the involvement of human enhancements on long voyages in space. At this early
stage of off-world exploration, we cannot anticipate all the types of physical and mental
difficulties that humans will encounter on journeys to Mars for exploration, settlement, and even
war, to the asteroids for mapping and mining, and to the outer planets for scientific research,
perhaps on Europa. However, we suspect that neuroplasticity, while substantial, may naturally be
just barely able to support human space travel with current technologies and propulsion systems.
An early finding is that humans may be unable to function for very long periods of time in the
environment of space or a microgravity planetary body without loss of bone density and muscle
tone. Gravity lower than Earth’s is debilitating in ways we are just discovering. We have written
elsewhere [6] that human enhancements will be necessary because the environment of space is so
harsh. Space has no atmosphere, water, or food. Travel for long distances may produce a sense of
monotony and ennui. There is little for the non-scientist to do, and according to analog
experiments, friction can arise among crew in tightly confined spaces, in new and restrictive
spaceships and in space colonies [7], [8], [9].

Studies of astronauts show that their brains change after spaceflight, and some disabilities
ensue that are related to the inner ear, balance, walking, and other faculties [1], [10]. Studies of
long-duration spaceflight (still less than a year, usually) already show harmful and lasting effects that can be traced, in part, to postflight increase in brain ventricular volume [2]. Kramer and colleagues [3] demonstrate that because of cerebrospinal fluid expansion and other effects such as a deformed pituitary, consequences such as changed ocular structure and function can possibly last for years after a return to normal gravity or be permanent. Intracranial pressure is being researched further because volumetric expansion of cerebrospinal fluid lasted up to a year into recovery, “suggesting permanent alteration” [1, p. 1].

Neuroplasticity is an important human trait, but it surely has its downsides. As research results accumulate on the possibility of permanent negative sequelae, concern grows, and with good reason. This is hardly an environment in which the “upsides” of human neuroplasticity are being touted, and still, those advantages to the human species must be understood and kept in context for future research. The very neuroplasticity that is causing early astronauts so many problems may allow later astronauts to be flexible, adaptive, and recover with remediation, or to be better prepared with human enhancements.

Sometimes, repeated exposure to space lessens the negative effects, suggesting a kind of adaptation, but at this juncture, researchers are unsure which human faculties are affected most and how severe the consequences are [1], [4]. With further research, it will be possible to plan and implement human enhancements that can counter some of these effects. In the meantime, we focus on locomotor and sensory embellishments that allow crew to accomplish mission goals.

Physical flexibility characterizes all the greater apes—a line from which humans descended in the late Miocene. Plasticity, and especially neuroplasticity, persist beyond childhood and adolescence into adulthood in some ways [11], [12], making the space traveler’s physiology and neurology changeable and amenable to remediation [13, pp. 167ff]. Other species could easily
substitute for us. The Arctic ground squirrel would likely survive a long hibernation—a fact not yet proved for humans—but that species could not plant a flag or know why it was so important to do so, in either practical or metaphysical terms.

On reflection, the logic and desirability of the installation of human enhancements, including bioengineering the human genome and medication of crew to counter the negative effects of spaceflight, emerge with clarity and certainty. Enhancements will allow humans to explore and settle the solar system. Without them, the species cannot, not for many centuries.

Therefore indirectly, neuroplasticity provides an avenue for remediation of the sequelae of spaceflight, through human enhancements.

2.2 Complex Evaluation Frameworks

Evaluation of human enhancements for spaceflight will involve complex assessments based on societal, governmental, and commercial goals—sometimes all at once. Comparison of different options for human enhancements will rely on measurements of safety, efficacy, and risk that have a variable knowledge base upon which to rely. Human enhancements emerging from rehabilitative medicine have a relatively good baseline of results, but many other relevant fields do not. For example, psychiatric medications delivered by nanotechnologies rely on limited research, and often, only on animal models. Furthermore, difficult decisions will be required when social values and commercial goals come into conflict. When varying cultural views on human enhancements come into play, they will add to already complex issues of evaluation, even more than thorny issues in the evaluation of pharmaceuticals.
2.3 Comparative Assessment of Human Enhancements

It is important to assess human enhancements collectively in a rigorous evaluation research framework so that space crew, program managers, funding agencies, companies, and the public understand the decisions involved. All stakeholders must buy into a rationale that the survival of human crew in a dangerous environment remains the goal, including achievement of goals for missions that are extraordinarily expensive.

For research on human enhancements to be most productive, a comparative framework that uses the same relative scales will be best. Human neurology allows this. CRISPR genetic engineering techniques can help to lessen the effects of bone loss in space, which will be substantial on a long voyage to Mars [6], [14]. However, will changes at new and different locations on the human genome be preferable? Will weight-bearing exercise be an adequate precaution before spaceflight? Will genetic changes and weight-bearing exercise together provide better protection on long space voyages? What of induced torpor? Will bone loss be more or less after torpor, and, will deep hibernation prevent it? These are the types of questions that should be asked. The answers will determine whether, for example, miners can emerge fully functional, able to dig for the precious metals on asteroids that are needed back on Earth for fine-tuned electronics or medicines. The stakes are high: life, itself, functionality of crew, national pride, and profits.

Risk-benefit analysis will operationalize the goals of a space program, whether based on exploration, settlement, commerce, or a combination. If space mission goals derive from aspirations of nation states, they must be congruent with their credos, and if they are based on commercial goals, then they must not stray too far from the standards and practices that protect employees and contractors. When human enhancements have adverse effects, they must strike a
balance between the value of a human life and value to the space mission. If human enhancements are too punishing to the human mind, brain, and body, then they become weapons or punishments, and they cease to be enhancing. Most dangerous may be the human enhancements that are addictive or that earthbound populations covet excessively and that lead to dangerous “markets.” All these factors could figure into a risk-benefit analysis.

Cost-benefit analysis will follow, and the risks, costs, and advantages weighed by program planners and space medicine boards. Given the vast array of human enhancements implied in Figure 1, the normalization of standards and measurements for all types of human enhancements will have enormous value. Reporting of results to governments and company officials must be in a format that is comprehensive, comprehensible, and useful. Comparability of enhancements will give administrators political cover if they need to explain why risks were taken and lives regrettably lost. Evaluation protects program managers from accusations of being biased, foolhardy, or too ambitious. Crew will have information they need to make decisions about a specific space mission. Not everyone will want to wager everything for fame or gain, but some will. Curtailing ambitions may be difficult, and all these thorny issues may lead to a black market in human enhancements.

Human spacefaring programs will consider a wide range of enhancements. Many are impossible to anticipate because the sequelae of long-term spaceflight are still largely unknown. Which human reactions to space will be untenable to society or inconsistent with a company’s “bottom line”, and which will require protective regulation for the safety of crew? Human enhancements will alter the human genome and its resulting cognition, at least for some crew. Viewing these diverse changes as a single set of alterations that must be tested, evaluated, and vetted has great value.
2.4 Risk-Benefit Analysis Involving Neuroplasticity Poses Methodological Challenges

Some see neuroplasticity as a bothersome “vestige” from another phase of human evolution, when the lifespan was still expanding to make adolescence longer and give humans time to learn advanced neurocognitive skills, like complex decision making that mixes scientific and values-based criteria—our own inborn, risk-benefit analysis. It will be important to avoid curtailing a trend in evolution by considering neuroplasticity \textit{de facto} dangerous, “fixing” it, perhaps unnecessarily, and rendering crews less able to think creatively.

Evaluation methods must ideally incorporate neuroplasticity’s inherently complex features, integrating its benefits and drawbacks, as well as social, political, and moral aspects, and perhaps, in the end, cost issues in an analysis of prevention and remediation options. Risk-benefit is not cost-benefit analysis, and there are values embedded in all variables. Because of neuroplasticity’s drawbacks and advantages, risk-benefit analysis, instead of beginning from a solid and sure platform, must \textit{begin} with a variable assessment of what is valued, what is needed programmatically, and then, in the end, what can be tolerated by astronauts, program managers, companies, and the public. Methodological consistency could allow comparisons between types of neurological deficits, both by themselves and in a context of multiple human enhancements.

If the costs of managing neuroplasticity mushroom or dangers to human neurology become excessive, then spaceflight for exploratory or entrepreneurial purposes will change. Human enhancements may then seem a better option.

The overall task is comparable to the assessment of the upsides and downsides of pharmaceuticals. Some robust, creative schemes have been developed. A well organized approach by Mussen and colleagues defines seven steps: (1) establishment of the decision context; (2) identification of the options to be appraised; (3) identification of the benefit and risk
criteria and organization in a value tree; (4) assessment of the performance of each option against the criteria; (5) assignment of a weight to each criterion using swing-weighting; (6) calculation of the weighted scores at each level and calculation of the overall weighted scores; and (7) a sensitivity analysis [15]. They go on to define 10 benefit criteria and 10 risk criteria for their targets, in this case, drugs; a value tree for a risk-benefit assessment; a meaty consideration of weighting; and a discussion of the public and programmatic utility of risk-benefit scores. A comparable analysis for neurological changes in response to spaceflight would involve different definitions of variables, as well as risk and benefit criteria. An analysis of different human enhancements would, as well.

Research of this type is a great deal of work and it lies in the future. Comparative assessment of neuroplastic changes in space will be difficult until a better knowledge base is available. A hanging issue is whether evaluation of remedial efforts should address “quality of life,” which is a concept that has achieved good metrics in modern societies, but almost loses its meaning in space or on Mars. Or does it?

How much neuroplasticity can the human body withstand in space? How much will kill an astronaut, and how fast? How much will save his or her life?

2.5 Longer Missions Provide Methodological Opportunities

Expeditions to Mars and deep-space missions open an opportunity for development of risk-benefit methods. The core idea is to calculate benefit-to-risk ratios and convert them to weighted scores that can be compared and ranked. Wilson and Crouch [16] note the method uses a wide variety of techniques from many disciplines, and we would add, law and ethics. The contexts of earthbound clinical medicine and human spaceflight are utterly different, especially the basis on
which the acceptability of risk is determined. At present, the saving of trained human crew continues to be the main goal. That may change when space commerce blossoms, but the collection of health data will be important for commerce, too, because of the enormous investment and potential profits. Wasting human lives will be counter-productive and very costly. The ethical conflicts of using human enhancements may then come to the fore. How many negative side effects will crew, companies, and the public tolerate?

While the collection of biometric data has been routine since Apollo flights, the human presence in space presents exceptionally challenging circumstances for the collection of evaluation data of a reflective, reactive, and self-conscious nature that could uncover relative degrees of neurological change and their importance to crew. In space, most data must be captured automatically and archived on Earth.

The time function of neurological change in response to spaceflight is largely unknown, and, it may be different for different neurological organs and tissues. Therefore, Low Earth Orbit (LEO) studies are important in order to begin gaining a handle on time, damage, and recovery, if any. Are the most damaging changes at the beginning, or only after a relatively long duration spaceflight? Do the early changes abate, reverse, or worsen?

2.6 Long Duration Exposure to Space, Weightlessness, and Hibernation
Our current era anticipates robotic expeditions to the surfaces of the Moon, Mars, and Near Earth Objects (NEOs) for the kinds of reasons given by Szocik [17]. However, the dream remains: exploration for its own sake, and the prospect of profitably mining resources to bring back to Earth. What calls this dream back into harsh reality are the anticipated, and unanticipated, human
neurological sequelae of long-duration spaceflight. Just how long will exposure to the conditions of spaceflight be? What is safe and what is not?

That depends on the mission and its timing. In Space Policy Directive-1, in 2017, NASA outlined an expedition to Mars. It first involves a return to the Moon, and somewhat beyond, to develop the necessary technologies for long-duration projects. Then, the roundtrip journey to Mars in the Deep Space Transport (DST) would take about three years, including some 300 days orbiting the planet, so just over a year in traveling one way [18]. The one-way journey would lengthen to a year and a half if the lowest energy path to Mars (a Hohmann transfer orbit) were taken. This option would require about 500 days of waiting on or around Mars to achieve the next lowest-energy transfer window, so all-told the round trip would take five and a half years.

There are several other serious projects for human expeditions to Mars: ESA’s plans with Russia, Elon Musk’s SpaceX, projects at Lockheed Martin and other space businesses, which mostly use the Moon as a gateway to Mars, and the “crowdfunded” Mars One. The mission of NASA’s Orion Multi-Purpose Crew Vehicle aims at longer periods in space [18]. Such cislunar orbits seem a desirable way to prepare crews for their eventual trip to Mars, if favorable adaptations in an individual can indeed be built up from previous flights. This possibility remains an important question for research. Still, the lengthening time in microgravity will probably extend the anticipated neurological sequelae, giving some negative effects and some positive adaptations. Can we anticipate enough of them to equip crew with the right human enhancements?

While present concerns are directed to Mars, serious thought is being given to mining asteroids as a resource. The C-type asteroids have water and fertilizer components. S-type have numerous metals, including rare metals. M-type are rare but have up to 10 times more metals
than S-type. The transport back to Earth of rare minerals, such as the industrially precious platinum group (ruthenium, rhodium, palladium, osmium, iridium, and platinum), remains a challenging entrepreneurial proposition because of its high cost and technical mining problems. These include the correct identification of resources, their extraction, and return. However, the ASTRA Team students of the International Space University, Strasbourg [19], produced an optimistic roadmap for overcoming these problems, and the Colorado School of Mining is among the first in the field with doctoral level courses in Space Resources. These programs make it likely that Near Earth Objects will be the first targets of space mining, including the prospect of towing some NEOs back closer to Earth, as proposed in the now defunded Asteroid Redirect Mission [18], (cf. a critique by Binzel [20]).

The value of asteroids much farther out in the main asteroid belt would seem to be for various construction projects and for propulsion refueling by crewed expeditions to the outer planets of our solar system. These asteroid trips probably involve several years in a spaceship, while a one-way trip to the Jupiter moons would take five years with present technology. More powerful acceleration and retardation with new propulsion systems would shorten these times. For now, this is the scenario in which hibernation for the crew looks like a solution to reducing stress in transit and limiting consumption of precious resources. Suspended animation refers to full cryo-preservation and restoration, and while it has been examined in experiments with animals, it is indeed for the future. However, an inactive torpor state induced by mildly lowering body temperature is already used in medical practice and being researched by NASA [18]. Controlled hypothermia like this is helping recovery from brain surgery for up to two weeks. If used longer than that, bones and muscles begin to atrophy. A possible limit is duration, as well as
the procedures for safely taking humans in and out of hibernation [21]. These are all currently under study.

Cognitive function in animals and humans does not seem impaired by the types of induced torpor and hibernation researched to date, or the durations studied. This will be a critical factor for the moment when a spaceship pilot needs to take over a landing on an asteroid or moon. A landing by artificial intelligence is currently being developed by NASA, but it can fail, as can other spaceship maneuvers, so it is important to maintain human mental acuity. It may well be true that crew can develop an increased ability to withstand hibernation, just as repeat spaceflights have indicated an increased adaptation to microgravity [4]. The species’ neuroplasticity would be useful in these circumstances.

Bringing the dreams of science fiction into science fact is what modern and ancient humans have done through technology for thousands, even millions of years. Neuroplasticity will be a key to successful long-duration space travel and habitation of other worlds, and research on it will have worthwhile and surprising consequences for medical and health research in the future.

2.7 An Epidemiology of Spaceflight

With a view toward the future, it is not too early to begin thinking about an “epidemiology of spaceflight.” There are only a few astronauts and cosmonauts who have stayed in space longer than six months, on the International Space Station. The longest human mission in space has lasted only 437 days, for Russian cosmonaut Valeri Polyakov [17]. The numbers will surely increase rapidly when tourists, astronauts, the military, and the crew of private entrepreneurial concerns access space and Earth’s moon. Before this outflow of people, it will be advisable to have warnings of the most dangerous neurological effects of space on humans. We now have just
the vaguest notion. Without the data collection involved in this epidemiology, reliable risk-benefit assessment will remain difficult.

3. Neuroplasticity: Background on a Human Biological Trait

3.1 Neuroplasticity as a Foundation for Human Enhancements

Evolutionary, developmental, and genetic perspectives on human neuroplasticity can help to frame today’s research questions, increase benefits for future space crew, and eventually reduce neurological deficits caused by spaceflight. Figure 1 indicates the varied knowledge base available for development of human enhancements to counteract the deficits. Human enhancements deriving from these fields can be used, to an extent, because of humans’ high level of plasticity, especially, neuroplasticity. *Homo sapiens* is a very flexible, adaptive species, in part because of anatomy and physiology, but also because of culture. Human enhancements as a group draw on all that flexibility. To date, researchers have approached neuroplasticity as a source of altered neurology in spaceflight, and so, with a negative cast. Researchers of human enhancements have sometimes approached them with an overly optimistic view, failing to consider the possible risks to crew and negative consequences for society.

In this, both a theoretical and a policy-relevant paper, we suggest a slightly modified scientific paradigm on both neuroplasticity and human enhancements for spacefaring, because the questions researchers ask can affect the type of data collected and the interpretation of findings. It is important to include views on human neuroplasticity and human enhancements that consider their negative, neutral, and positive effects before, during, and after spaceflight.
3.2 Research on Neuroplasticity after Spaceflight: Space Adaptation and Positive Sequelae

Expansion of a research paradigm for neural plasticity in spaceflight includes the following: (1) From a biological perspective, an evolutionary understanding of neuroplasticity's nature and function in our species; (2) From a medical perspective, all levels of human biological organization, from genomic to histological, to organ systems, neural networks, neurological systems, and to groups of humans and their joint social functioning that allows them to complete cooperative work assignments in space; (3) From a research perspective, avoiding pre-judgements that the changes due to neuroplasticity in space will all be negative, and a consideration of possible neutral and positive sequelae in humans, and, (4) From the perspective of program support and financial investment, an understanding that neuroplasticity in spaceflight, if problematical, is amenable to remediation, depending on the specific neurological feature changed and the risks of remediation, especially with human enhancements.

3.3 Normalizing the Research Paradigm

It will be useful to assess all potential human enhancements collectively, using common metrics, and consider life-saving human enhancements for humans who travel in space in a comparative context. In this way, an increasingly wide range of surgeries, mechanical and tissue implants, medications, and consciousness-altering drugs to lessen the effects of ennui and interpersonal friction on lengthy space voyages [22], [23] can be evaluated using common yardsticks. Research results can then provide a rationale for use, or not. This may not be entirely feasible for all modifications, but the approach is comparable to the comparison of the efficacy and safety of different pharmaceuticals.
3.4 Research on Neuroplasticity

“Neuroplasticity” is a term now used for a still-small set of physical, mental, and behavioral alterations involving the human neurological system, after time in space. With additional research, this set of changes will grow enormously. To date, changes were identified in crew returning from the International Space Station and individuals in spaceflight simulations. Findings from these studies have long shown that neuronal plasticity is responsive to weightlessness [24], [25], [26], [27], [28]. Until work on space programs began, research on hibernation—an important factor that potentially impacts neuroplasticity—was investigated primarily in animal models, especially the Arctic ground squirrel, by Kelly Drew, a pharmacologist with the University of Alaska Fairbanks, and Alejandro Rabinstein, a neuroscientist at the Mayo Clinic. Hibernation in humans has been conducted primarily by DARPA for military purposes. Martin Braddock points to the physiological basis for studies on hibernation: “The potential for human beings to be in a state of hibernation or stasis has long been recognized from the animal kingdom” [21]. Weightlessness and hibernation are not the only features of spaceflight to potentially impact (or be impacted by) human neuroplasticity, but they are important in early phases of space exploration. However, to achieve the most efficient human functioning, it is likely that remediation will be supplemented, or achieved at all, by human enhancements.

Failure to consider the consequences of spaceflight on the human neurological system, the human mind and behavior, risks mission failure, loss of life, destruction of costly equipment, waste of resources, and for some, loss of profit. Success in anticipating neurological changes allows for remediation or even improvements of human performance based on some neurological changes—especially if deficits are met squarely with the use of human enhancements.
Recent research suggests that the brain appears to change after “long-duration spaceflight” — still generally far less than a year. However, the nature and extent of changes remains largely the subject of future research. As early as 1994, Newberg summarized a complex picture that others have later confirmed, i.e., a combination of adaptations to the space environment, such as new proprioceptive responses, but also some maladaptive changes, for example, the disruption of circadian rhythms or even neuronal damage[29]. Later researchers documented other concerns in more detail. Although Newberg’s summary analysis was focused on the “central nervous system,” by 2016, Demertzi and colleagues demonstrated that, while intervening research dovetailed elsewhere, their results also focused on the CNS. They write that, “For the first time, …we found significant differences in resting-state functional connectivity between motor cortex and cerebellum, as well as changes within the default mode network” [1]. We are learning more and more about the importance of the joint functioning of networks, so their connectivity is critical [30], [31].

The risks of spaceflight, space stations, and off-world environments for the human mind and body will be emerging for centuries to come. Unless aided by artificial gravity that is still in an experimental stage, humans could spend years in weightlessness, or in and out of weightlessness. Crew, including military personnel and mining crews, could experience long periods in the reduced gravity of Earth’s moon, Mars, and the asteroids, which are small and have little gravity. Therefore, it is essential to understand human neuroplasticity and what the concept means for our species. Are we gifted or are we hobbled by a high level of neural plasticity that extends well into adulthood? Or both?
3.5 The Nature of Human Neuroplasticity

The human brain returns from space “changed”, and while this can be alarming [32], [1], [33], it is not unexpected if the evolutionary origins of neuroplasticity are appraised [34], [35]. Furthermore, neuroplasticity offers certain benefits. Sensory substitution was one of the early areas to be considered a positive result of “brain plasticity” [36]. Paterson [37] suggests a positive function for neuroplasticity in tactile-visual sensory substitution (TVSS). A systems and engineering perspective by Anderson and Finlay hints at how neuroplasticity could be seen as advantageous for an experience as disruptive to an Earth-evolved biological system as spaceflight. A very flexible, distributive system would be favored by natural selection in human evolution:

“Mounting evidence… suggests that brain elements are used and reused in multiple functional systems. This variable allocation can be seen in short-term neuromodulation, in neuroplasticity over the lifespan and in response to damage… Here we highlight the interaction between evolutionary and developmental mechanisms to produce distributed and overlapping functional architectures in the brain… Natural selection must preserve behavioral functions that may co-locate in variable amounts with other functions.” [38]

In these scholars’ work and the neuroscience literature, in general, there is an increasing focus on brain networks that together have variable functions depending on the cognitive capacities needed by humans—capacities that could number in the “thousands” [39]. Neuroplasticity helps humans adapt to new environments partly through an ability of the brain to switch combinations of networks and draw on resulting cognitive capacities.
The ability of neural networks to manage the human experience of spaceflight should not be underestimated. Humans are naturally well equipped by flexible, multipurpose neural networks. However, they will encounter difficulties, and neuroplasticity, while it can cause problems, also provides a ready biological context for introduction of human enhancements that will compensate for these and other difficulties.

3.6 Evolution of Neuroplasticity

Neuroplasticity stands an excellent chance of emerging as a “key innovation” as defined in the Extended Evolutionary Synthesis of modern theory. A key innovation is a new and unusual phenotypic trait that allows, possibly encourages, radiation and success of a taxonomic group, in this case, the genus Homo. Through either genetic drift or natural selection, and probably both, neurological plasticity became fixed as an important trait on the human line. Neuroplasticity emerged long before it would ever be examined as an important factor in spaceflight.

Study of human evolution with an eye toward the future of spaceflight is a new concept. Yet, it will be useful to consider neuroplasticity throughout its evolutionary timeframe and with an understanding of its original purposes in the genus Homo. Neuroplasticity is congruent with many human biological traits that emerged on the human line that reflect “secondary altriciality,” i.e., an extended period of dependency beyond the perinatal period, theoretically so that youth and adults had sufficient time to master the higher neurocognitive skills that are needed now, for example, by crew on a space mission. The lifespan was already lengthening and brain size was increasing in the large, ancient ape population from which the human line branched. Human evolution simply accentuated those trends enormously, and with results that can benefit the future of human spaceflight.
It would not be obvious for many thousands of years that neuroplasticity could also cause problems for space crew. Still, it could be argued that human neuroplasticity fundamentally enables human space exploration, leaving Earth, and surviving far into the future as one in a series of species in the genus Homo—its current status. A less plastic genome, an inflexible developmental biology, and fixed, inherited, complex behavior patterns would require massive enhancements for spaceflight. Imagine sending a sentient bird to space. Yet, humans are flexible, very plastic, and they appear primed for the task of space exploration, to an extent and with a little help from human enhancements.

“Plasticity” means different things to the neuroscientist, the paleobiologist, the geneticist, and the space medicine specialist, but all meanings appear to intersect at some very high level in the human species. They can be traced to the development, organization, and functioning of the human nervous system, which is changeable. Evolutionary neurobiologist Leah Krubitzer writes that plasticity is a capacity to be “molded or altered,” and a “capacity to change” [40]. This suggests that plasticity allows for human neurology to change, but the whole remains coherent, without a loss of unity or orderliness. In human neuroplasticity, there is purpose in changeability: It is a response to the environment, including both earthbound environments and off-world environments like the International Space Station [10]. Neuroplasticity’s perpetuation into adulthood provides an ability to recover from injury, even in old age. Longevity and senescence, like a high of neuroplasticity, are other unusual human biological traits consistent with a lengthened developmental trajectory [41].
3.7 Developmental Basis for Neuroplasticity

The social functions of neuroplasticity in modern adult humans become clear when they are viewed in evolutionary and cross-species context. In humans, some juvenile traits are retained into adulthood, like a down-regulation of aggression. Humans remain flexible, curious, creative, and available for neurological remediation. They are better able to work closely with other adults because the easy sociality of childhood is perpetuated.

A reduction in aggression and an increase in intelligence to manage aggression were important in human evolution so that adults could work well together. Modern chimpanzees have no problem feeding and socializing as juveniles, but when they reach adulthood, chimpanzees, like gorillas, become more aggressive and/or solitary. To achieve the lower-tension sociality of humans or bonobos, juvenile traits were retained in adults of both species [42], [13].

Research on humans and chimpanzees suggests that plasticity emerges neurologically partly in response to culture, and that conversely, cultural learning in humans (but not chimpanzees) is dependent upon it. Gómez-Robles and Sherwood find that, “Plasticity is the propensity of the brain to be molded by external influences, including the ecological, social and cultural context…it has been only recently that scientists have started discovering the more pronounced plasticity of human brains compared to our close relatives” [34].

Neuroscientist Michael Gazzaniga and colleagues note that “different regions of the human brain develop at different rates, with association areas lagging behind sensory and motor structures” [43]. Humans have a lengthened period of maturation in pre-frontal association areas. Comparisons with chimpanzees suggest that plasticity is greater for parts of the human brain related to higher neurocognitive traits. They evolved late.
3.8 Neuroplasticity in *Homo sapiens* and *Homo neanderthalensis*

Plasticity is an evolved source of human adaptive capacity. It is a set of inborn mechanisms that enable humans and other mammals to accommodate to new environments. Genomic research suggests a lower level of neural plasticity in other species of the genus Homo, such as the Neanderthals, compared to *Homo sapiens*. Archaeological findings suggest less behavioral flexibility, a smaller home range, and the absence of Euclidean navigation, a cognitive capacity largely enabled by expanded parietal lobes [44], [45]. Modern humans and Neanderthals have different skull shapes in the parietal areas. Human skulls are expanded in the parietal areas, the frontal lobes, and the cerebellum, giving rise to our globe-shaped skull [cf. 13].

Oddly enough, interbreeding with other early humans, such as Neanderthals and Denisovans, may have helped humans to achieve a high level of neuroplasticity by providing additional genetic variability. Today, humans are remarkably similar genetically, and they still have an “effective population size” (a measure of population variability and quality) of 10,000, in spite of a census population in the billions.

Neuroplasticity differentiates humans morphologically from their most closely related living species, members of the genus Pan, including the chimpanzees (*Pan troglodytes*) and the bonobos (*Pan paniscus*). Theory is emerging on the mechanisms whereby culture exerts a great influence on human neurology. Gómez-Robles and Sherwood write that, “Analyses of large samples of chimpanzee and human brain MRI scans have shown that heritability for cortical organization in humans is low, whereas in chimpanzees is high…which points to the greater level of environmental influence in cortical organization in humans” [34, p. 4], [cf. 46].
3.9 Genetic Origins of Neuroplasticity

Findings suggest that human plasticity is determined by a wide range of genes. Yet, it meets the requirement of being a “reliably produced” biological trait [47] whose high level distinguishes modern humans from closely related species. Neuroplasticity’s role in changing the human nervous system so that advanced neurocognitive skills can be learned involves humans theoretically in their own evolution [48], [49], [50], [51].

For human neuroplasticity to be captured and reproduced by our genome over evolutionary time meant that it had important functions. In modern humans, maturation of many complex cognitive, linguistic, social, and cultural capacities does not occur until the late teen years and some do not appear until the twenties or thirties. Some of the interconnections between neuroplasticity, neurological developmental patterns, maturation, and specific social and cultural requirements for Homo sapiens all revolve around the species’ tendency to mature late and variably. Theory is developing as to why this developmental trajectory emerged in the human species, including a hypothesis that it is an advantage for the human social group for the onset of full cognitive capacities to be delayed in youth [52], [53]. The pre-frontal cortex naturally matures late, and humans remain cognitively immature until around twenty or thirty. Without some aspects of neuroplasticity remaining until that time, full development would not occur. Neuroplasticity remains useful until humans can master complex decision-making, and moral and ethical thinking typical of their culture, and, they do. They are primed for it.

Sherwood and Gómez-Robles [35] diagram the evolution of major plasticity-related genes, and some of their sub-types, from the DNA of Neanderthals, Denisovans, and modern humans. Their work suggests that plasticity is indeed determined by more than one gene. These researchers discuss a human-specific, protein-coding form of the FOXP2 (forkhead box P2)
gene, which is shared with Neanderthals and Denisovans. There is a variety of FOXP2 genes in the vertebrates and the gene is often involved in some form of communication. When the human form mutates, individuals have a severe speech disability.

Interestingly, Wolfgang Enard and colleagues [54] have shown that the human FOXP2 gene increases plasticity in cortico-striatal circuits when expressed in the mouse model. Fisher and Scharff write that, “Converging data indicate that FOXP2 is important for modulating the plasticity of relevant neural circuits” [55]. It is important to remember this is only one gene.

Equally interesting details emerge on a second gene, SRGAP2 (SLIT-ROBO Rho GTPase Activating Protein 2), which is involved in human neocortical development, and may be involved in human plasticity [34]. As with so many human biological traits, plasticity has multiple coding and regulatory genes that guide its functioning phenotypically. The human regulatory FOXP2 is our species’ alone, although modern humans share the human protein-coding FOXP2 with Neanderthals and Denisovans. Regulatory FOXP2 may be the source of a very important difference, which enables modern human speech.

It is not surprising that speech is connected to plasticity. As a mechanism for the production of language, speech uses a symbolic system, as does mathematics, that is infinitely amenable to recombination. Aspects of speech rely on late maturation of the human neurological system, such as finely tuned features of social speech, persuasion, and negotiation. Social speech is refined in the later stages of human development.

3.10 Why Is It Important to Conserve Neuroplasticity for Spaceflight?

Human neuroplasticity has both risks and benefits by its very nature, irrespective of spaceflight. In relying on early influence from a rich cultural environment of emotionally involved caretakers
to determine *neural* organization, development can go sadly awry if that environment is not present or nurturing. The benefits of retaining some neuroplasticity into youth and adulthood means that recovery from certain types of neurological injuries and malfunctions during spaceflight is possible. Mental stimulation helps, along with medical routines that have been researched and continue to be identified for remediation of returning astronauts, and programs for crew with an upcoming spaceflight. Some regimens borrow features from treatment of spinal cord injuries [55], [56] and routines of physical activity, mental engagement, and diet address comparable problems in lifestyles of the aging [57].

Studies of vestibular function in the aging may shed light on neuroplasticity in spaceflight [58]. The neuro-chemical bases for neuroplasticity in humans have been examined, especially the roles of serotonin, GABA, and dopamine in the effects of drug abuse on neuroplasticity [59], [60]. As Borodovitsyna and colleagues remind us, “Neural plasticity plays a critical role in mediating short- and long-term brain responses to environmental stimuli. A major effector of plasticity throughout many regions of the brain is stress” [61]. Spaceflight involves periods of intense stress for humans, so they will be impacted. The question is whether remediation will suffice, or whether human enhancements will be used to prevent the detrimental effects of stress.

### 3.11 The Neuroplasticity-Intelligence Connection and Its Importance for Spaceflight

Theory suggests that human brain fold patterns may vary because of culture. Sherwood and Gómez-Robles carefully interpret the evidence to date, and point to a connection between neuroplasticity and intelligence:

> “At the time of birth, dendritic arborization and synaptogenesis are occurring at peak rate, which will extend well into the first few years of postnatal life…”


Shaw et al. (2006) found that children who scored the highest on an intelligence test had brains that were characterized by an especially prolonged phase of initial increase in prefrontal cortical thickness prior to the period of thinning” [35].

There is corroborating evidence by Fjell and colleagues [62], who report that changes in association areas correlate with results on cognitive tests that reflect intellectual ability.

If neuroplasticity is clearly related to intelligence, then efforts at remediation should be careful not to reduce it. If human enhancements are introduced successfully, in part because of human neuroplasticity, then it is of paramount importance that they do not damage that capacity, but perhaps enhance it. The ethics of enhancing intelligence are complex, and enhancements related to intelligence provide a good example of the need for in-depth evaluation.

It could be argued that robots should do the job of space exploration, because the balance between delicate human capabilities and their accommodation both to space and to human enhancements may be difficult. Still, remediation of changes to the brain and sensory apparatus after spaceflight should not reduce humans’ substantial neuroplasticity and intelligence. Late-developing association areas of the human brain are critical in planning, problem solving, and creativity, and these are all essential to human off-world missions. Anticipating problems and configuring possible solutions for space missions will be long and complex, but planners cannot anticipate everything. Crews in space will have to improvise, and evolution has gifted humans naturally with that ability.

Protecting human neuroplasticity may be a very good idea, if both its negative and positive consequences can be managed. That management may well entail the use of human enhancements, whose operation should lead to improved performance, but not at the cost of human intelligence and innovation.
4. Summary: Neuroplasticity, Remediation, and Enhancement, A Changing Perspective

The time has perhaps come when human plasticity, especially neuroplasticity, is purposefully explored and exploited for the purposes of improving the experience and performance of crew on space missions. We noted at the beginning of our discussion that much is at stake: exquisitely trained crew, men and women in the peak of health, sometimes lofty goals of exploration and at other times, handsome profit.

The foundation for the implementation of any human enhancement must be approval by Space Medicine Boards. Space travel will be dangerous, and sometimes the risk and benefits will array themselves in a complex manner. Unless nations and companies choose to explore space with robots, the choice of using any particular human enhancement will be based in part on the foundation of an agile, flexible, neuroplastic human species that evolved on planet Earth and is not accustomed to weightlessness and the harshness of space or other planetary bodies.

Human enhancements build on strength. They should not sap strength. Their net effect should be positive. Their rationale is mission completion, insofar as humans can tolerate their side effects. The agility, flexibility, and plasticity of the human species should provide a strong matrix for many types of human enhancements. There is already a great deal of research in some of the fields diagrammed in Figure 1, which will be a springboard to additional, future research on many more specific alterations to the human genome, body, brain, personality, and social functioning. All these areas are potential areas for enhancements to enable humans to tolerate long space voyages.

It is somewhat ironic that it is neurological deficits that called neuroplasticity to the attention of space medicine researchers. We see a future in which special capabilities for space mission
crew will be forthcoming, built on a platform of human plasticity, which evolved over millions of years to enable humans to use their highest neurocognitive assets.

REFERENCES


