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Research Article

Visualizing Chemistry. The Application of Chemical Imaging to Address Scientific Challenges in Space Research

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Abstract. Chemical Imaging helps to answer difficult questions, especially when those questions occur in complex environments. For instance, forensic neuroradiology plays an important role in the courtroom to understand a defendant's personality. But could this branch of science be essential in human exploration of space? Even if no emergency has happened so far, NASA established a partnership in 2002 with the U.S. National Institute of Justice to promote the knowledge of investigative techniques in the case of a crime being committed on a space mission. Based on forensic neuroradiology and behavioral genetics, this article presents a brand-new study protocol for creating security procedures designed to safeguard astronauts engaged in long-duration space travel. Since 2009 in Italy, some individuals have been prosecuted who, although convicted of murder, benefitted from reduced sentences through the verification of some genetic polymorphisms and Computed Axial Tomography (CAT), Positron Emission Tomography (PET), and functional Magnetic Resonance Imaging (fMRI) results which showed brain malformations that may produce manifestations of violence. The protocol specifically uses chemical imaging and behavioral genetics to show how cerebellar anomalies and biological markers predictive of criminal behavior can trigger impulsive reactions in response to stress. This protocol may prove critical when space agencies are evaluating candidates for extra-orbital flights of long duration.

Keywords. Chemical imaging, forensic radiology, NASA, behavioral genetics, space research.

INTRODUCTION

In 1958, President Eisenhower proposed creating a civilian space agency for the United States. After considerable congressional debate, the National Aeronautics and Space Administration (NASA) began its operations on October 1, 1958. No one could ever have foreseen what would occur over the next 50 years as humans discovered that the sky was no longer a limit and it is now about to enter a new era of space exploration with a 365-day stay on the ISS, the establishment of a lunar landing outpost, and the future missions to Mars and to a near-Earth asteroid (NEA).[1,2]

As missions to NEA and Mars are not just ordinary space flights, the analysis of physiological and psychological risk factors of past missions will not be relevant bases for predicting the risk factors astronauts may encounter during space flights.[3] At the Hawaii Space Exploration Analog and Simulation center, NASA concluded in 2016 a year-long study regarding the use on a shuttle of the forensic sciences utilized in examining crime scenes.[4] In fact, the probability of criminal conduct in space is not so remote. For instance, astronauts have carried weapons into space since the Soyuz flights in 1965.[5] Thus, forensic scientists are prepared to face the eventuality of assessing crime scenes and identifying evidence during space travel. So it is no coincidence that NASA established a partnership with the U.S. National Institute of Justice to implement investigative techniques for use in future crime scenes in space.[6]

Over the last two decades, several studies have been published regarding the impact of long-duration space flight on the health of crewmembers.[7] Moreover, while the physiological effects of space flight are well documented,[8] a paucity of knowledge exists on the potential behavioral and cognitive issues that can affect the astronaut's psychophysical performance during flights. For instance, the neurobiological consequences of long-duration space flight and long-term exposure to microgravity can lead to alterations in cerebral morphology (e.g. the Visual Impairment and Intracranial Pressure Syndrome) that are poorly understood.[9.10]

Even if no emergency has happened so far, we need to think the unthinkable: how would we deal with a catastrophic scenario during a long-duration space flight? In this paper, we present a study protocol that aims at certain security procedures designed to safeguard astronauts engaged in long-duration space travels. The protocol is based both on chemical imaging, e.g. forensic neuroradiology, to evaluating the cerebral regions whose anomalies can lead to antisocial behaviors,[11] and on behavioral genetics where it has been demonstrated how specific predictive biomarkers of criminal behavior can lead to an unpredictable response in very stressful situations.[12] These evaluations can be crucial for space agencies at a time in which space tourism is going to become an achievable dream.[13]

MATERIALS AND METHODS

NASA's Human Research Program has identified 32 space-related health risks associated with space flight and has listed them in the Human Bioastronautics Roadmap. The level of risk refers to three specific parameters: a 1-year tour of duty on the ISS, a month-long stay on the moon, and a 30-month mission to Mars. Health risk factors are then categorized into: (1) behavioral health and performance; (2) human health countermeasures (e.g., bone metabolism and physiology, nutrition, immunology, cardiac and pulmonary physiology); (3) space radiation; (4) space human factors and habitability; and (5) exploration medical capabilities. The risk factors have been rated as Controlled, Acceptable, Unacceptable and Insufficient Data. The Roadmap then highlights as unacceptable the risk of behavioral issues and psychiatric disorders.[14]

In 2007, NASA developed various health standards (i.e., Crew Health Concept of Operations and Medical Operations Requirements) directed towards "a healthy and safe environment for crewmembers during all phases of space flight".[15] A review of all the NASA health standards is conducted every 5 years or any time new scientific data suggest that an update is needed.

In addition to the standards described above, NASA has identified specific health criteria for crew selection including a medical screening and annual examinations reported in the Astronaut Candidate Program and supported by the NASA Aerospace Medicine Board.[16] It is worth mentioning that health risk and stressor parameters may be different from mission to mission. Concerning behavioral health and performance risks, NASA has identified three stressors associated with long-duration space flight: (1) adverse behavioral conditions and psychiatric disorders;[17] (2) performance errors due to fatigue;[18] and (3) performance decrements due to inadequate cooperation, coordination, communication, and psychological adaptation within a Team Gap.[19] These criteria were identified by analyzing observational data and experimental studies in analogous settings, such as submarine,[19,20] space simulations,[21] mountain survival programs and polar expeditions.[22]

It is important to note that behavioral health problems may be underestimated due to the reluctance of crewmembers to report them.[23,24] In 2000, a survey documented a 2.86 per person-year incidence of behavioral problems among the 508 astronauts engaged in space shuttle flights between 1981 and 1989.[25] In 2009, observational information collected for 28.84 person-years described anxiety and irritability as the most common behavioral symptoms (0.832 cases per person-year).[26] Furthermore it was pointed out that behavioral health issues are frequent during long-term periods of isolation and confinement.[27] A 2004 study reported a 5.2 percent probability of behavioral issues in aspiring astronauts after extended stays in Antarctica. Among the most common risk factors of behavioral health problems are mission duration, circadian rhythm disorders and microgravity effects on human physiology, social isolation, cultural and organizational issues and personality traits.[28] Risk management procedures have focused on providing social and psychological support to crewmembers through ground control. However, even if these countermeasures have proved to be effective on the ISS, it is unknown whether they could be useful during long-term space flights at greater distances from Earth.[2] Cognitive and psychiatric tests are administered during both the astronaut enrollment procedures and the annual medical examinations.[29] Neurocognitive and behavioral genetic testing have also been developed, but they serve mainly to point out phenotypic and genotypic variations to manage sleep-wake disruptions during space missions.[30] To date, few policies have been established for long-duration space flights. In analogous settings, the National Science Foundation's Division of Polar Programs require a psychiatric evaluation conducted by a civilian contractor of all aspiring astronauts engaged in winter-over duty at Antarctica's Amundsen-Scott South Pole and McMurdo stations. Limits have also been placed on the number of continuous seasons a candidate can stay at the same station.[29] Astronauts are then informed that ordinary social and personal problems can become clinically significant during periods of extended isolation and confinement. For instance, the Mars Society conducted a 4-month simulated Mars exploration mission at the Flashline Mars Arctic Research Station in 2007. Analyzing the questionnaires that crewmembers completed on five different occasions during the simulation, scientists found an increase in stress factors as well as higher levels of excitement, loneliness and tiredness. These results thus prompt serious questions about psychological issues during missions to the outer solar system where a mission's total duration is expected to last 10 years or more (e.g., interstellar travel to the Oort Cloud, a broad spherical shell of comet nuclei located 0.63-0.94 light years away from the Sun).[31]

These kinds of human expeditions will cause astronauts to undergo psychological and interpersonal stressors that they have never before experienced, such as an unknown level of monotony and isolation, impossible real-time communication with the Earth, which will even disappear from their view. Such would be the case of missions to Mars where a crew of six or seven people would be on a space flight lasting at least 2.5 years. For the very first time in human history, they would experience the "Earth-out-of-view phenomenon". Gazing at the Earth has been one of the major positive factors of being in space for astronauts. Its absence could lead crewmembers to an increased sense of isolation, emotional instability, hypersensitivity, depressive reactions, and possibly psychiatric disorders.[32]

As has already been mentioned, many unknown health risks may influence long-duration space flight. In this regard, it is noteworthy to emphasize that chemical imaging can make a positive contribution to forensic space research. For instance, a recent clinical survey tested via fMRI the neuronal functions of a 44-year-old male cosmonaut engaged in a long-duration space flight (169 days) on the Russian segment of the ISS. Even if his physical state and performance showed no relevant anomalies, the fMRI scans indicated abnormalities in the vestibular and motor-related cerebral regions.[10] Moreover, results from the MARS105 study have shown a deterioration in the astronauts' psychological state during a long period of confinement, which was accompanied by a decrease in brain cortical activity.[33] Again, in a study carried out using low-resolution brain electromagnetic tomography (LORETA), neuropsychiatrists have demonstrated how the microgravity phases of parabolic flights induce changes in frontal lobe activity, a cerebral region that is involved in the regulation of emotional processing.[34]

Despite what has been described above, the contribution of forensic neuroradiology and neurobiology to space research seems to be underestimated. Therefore, increased focus on brain imaging and behavioral genetics can lead to the development of adequate countermeasures to safeguard astronauts involved in long-duration space missions

Brain imaging

Cognitive neurosciences have as a study subject an understanding of the mechanisms that are the basis of human aggressivity; they find their correspondence at an organic level and in particular cerebrally. The main objective of this branch of research is to investigate violent behavior in humans by studying certain cerebral areas using neuroimaging techniques, which constitute a major source of scientific acquisition in the neurocrime field. It follows that cognitive neurosciences, linked to the growing technological development in the field, are destined to evolve over the next few decades influencing such fields as psychiatry, forensic psychology, and criminal law in studying the *mens rea*.[35]

The development of multiple imaging techniques provides powerful tools to probe multiple aspects of brain anatomy. New technologies not only allow the study of structural features but also reveal brain connectivity, neurotransmitter receptor profiles, and other important aspects of brain function. These sophisticated imaging systems are divided mainly into the following areas: EEG (electroencephalography); CAT (computerized axial tomography) scan; functional magnetic resonance imaging (fMRI); positron emission tomography (PET); single-photon emission computed tomography (SPECT); and magnetoencephalography (MEG).

In detail, EEG allows direct assessment of the brain's electrophysiology by displaying the temporal and spatial pattern of the neuronal populations generating the underlying neuroelectric and neuromagnetic fields. Given its temporal sensitivity, EEG is useful in the evaluation of dynamic cerebral functioning such as suspected seizures and unusual spells.[36] CAT scan is a computerized X-ray imaging technique where a motorized X-ray source rotates around the circular opening of a gantry, producing signals that are then processed by the machine's computer to generate 2-D cross-sectional tomographic images (often called "slices"). The thickness of each slice usually ranges from 1-10 millimeters. When the number of desired slices is collected, image data is recorded in DICOM format and images can be displayed separately or stacked together by the computer to produce high-resolution 3-D images (c.50μm).[37] CAT scan and magnetic resonance imaging (MRI) have allowed for the first time the noninvasive evaluation of brain structure. In particular, fMRI is a modern noninvasive imaging technique to measure and localize specific functions of the human brain without the application of radiation. Indeed, fMRI takes advantages of the differences in magnetic susceptibility between oxyhemoglobin and deoxyhemoglobin. When a task is performed, oxygenated blood in excess of the amount needed (luxury perfusion) is delivered to the active area. The difference in magnetic susceptibility between deoxyhemoglobin concentrations and oxyhemoglobin concentrations creates the signal in functional imaging. Brain function is indirectly assessed with high spatial resolution via detection of local hemodynamic changes in capillaries and draining veins of the so-called functional areas, e.g. regions of the human brain that govern motor, sensory, language, or memory functions. Thus, fMRI not only offers a variety of novel options for research but also opens up a new diagnostic field of neuroradiology, by shifting paradigms from strictly morphological imaging to measurement and visualization of brain function.[38] Other frequently applied methods for the identification of functionally important brain structures are PET and SPECT, which detect changes of cerebral blood flow and glucose metabolism. Most significantly, PET measures generally reflect the functional biochemistry and physiology of the brain. This is accomplished by injecting radioactive isotopes that have short half-lives. Isotopes used frequently in PET research allow a variety of radiochemical approaches to ligand synthesis. Of particular importance, isotopes of carbon and nitrogen may be directly incorporated, and ^{18}F can be substituted for hydrogen or a hydroxyl substituent in many compounds without loss of bioactivity. Blood flow indeed increases in areas of the brain that are in heavy use and a fair portion of the injected isotopes will end up in the active part of the brain. As the isotopes decay, a positron is released. This positron will collide with an electron and they will annihilate each other, sending two photons, or γ-rays, in opposite directions. These γ-rays are picked up by the PET scanner, which then determines where they came from the brain. Tomographic techniques analogous to those utilized in CAT scanning, are used to reconstruct the image from the rays. The resulting PET images are spatial maps of radioactivity distribution within tissue slices.[39] SPECT is another nuclear imaging technique for imaging molecules, metabolisms, and biochemical functions of organs and cells, and like PET, the use of radioisotopes is required. As its name suggests, it involves the emission of a single γ-ray per nuclear disintegration, which is measured directly. Numerous single γ-rays are detected by rotating gamma cameras to reconstruct an image of the origin of the γ-rays, which identifies the location of the radioisotope. Before a test is performed, the patient is injected with a radiopharmaceutical that emits γ-rays and can be detected by the scanner. The most common radioisotopes used in SPECT are Iodine-123, Technetium-99m, Xenon-133, Thallium-201, and Fluorine-18. SPET scan is primarily used to measure the regional cerebral blood flow. One of its major advantages is that SPECT provides improved contrast between regions of different functions, and also give better spatial localisation and greater accessibility because it uses radioisotopes with longer half-lives.[40] Finally, MEG is the measure of magnetic fields generated by the electrical activity of neurons. When neurons are activated synchronously they generate electric currents and thus magnetic fields, which are then recorded by MEG outside the head. Once generated, magnetic fields are relatively invulnerable to intervening variations in the media they traverse, so they are not distorted by the skull, grey and white matter, and cerebrospinal fluid. But these neuromagnetic signals are extremely small, about 10^{-15} T. Thus, MEG scanners require superconducting quantum interference device (SQUID) sensors. To detect and amplify the magnetic fields, the SQUID sensors are bathed in a large liquid helium cooling unit at about -270°C. A magnetically shielded room houses the equipment and mitigates interference.[41]

The brain areas that are relevant to the present study are the amygdala, hippocampus, thalamus, midbrain, and prefrontal cortex. The amygdala is involved in predatory and affective attacks. The thalamus connects the limbic emotional areas and cortical areas. When activated, the midbrain manages impulsive aggression due to emotions.[42] The literature has found that reduced hippocampal function can be associated with high levels of psychopathy.[43] The hippocampus also plays a primary role in fear conditioning and in emotional responses.[44] The almond-shaped amygdala is also involved in the generation of emotions. An amygdala dysfunction leads to manifesting impulsive, even violent behaviors.[45] For instance, a decrease in the amygdala's volume equal to 18% can instead be the basis of sociopathic behaviors.[46] As regards the midbrain, a disorder in the posterior cingulate cortex can trigger anger. In addition, it distorts the possibility of understanding how this behavior can influence others.[47] The same applies to the anterior cingulate, the cerebellar anatomical region designated to inhibit automatic and instinctive behaviors and to regulate instinctive reactions.[48,49]

The most important evidence capable of translating into reality the literature attesting to the biological nature of the anti-social acts is found in the judicial practice of both Italian and US criminal trials, where a reduced sentence was imposed on the basis of the confirmation of anatomical differences in the defendant's brain as well as genetic anomalies that were capable of influencing the behavior of individuals, causing them to carry out heinous behaviors against their fellow humans.

US criminal trials

The use of bioscience in criminal cases dates back to the early 1980s when chemical imaging and behavioral genetic evidence began to enter US courtrooms. On March 30, 1981, John Warnock Hinckley Jr. shot President Ronald Regan six times, also critically wounding police officer Thomas Delahanty, Secret Service agent Timothy McCarthy, and Reagan's press secretary, James Brady. When he was put on trial for his crimes, Hinckley was found not guilty by reason of insanity and confined to St. Elizabeth's mental hospital in DC. He was released in September 2016. The Hinckley case revolutionized the US criminal justice system introducing CAT scans as a useful tool for proving mental incapacity. The psychiatric David Bear explained to the jury that the defendant's brain scans indicated that Hinckley's sulci were wider than average, a feature that he had noticed in patients suffering from schizophrenia. The CAT scans bolstered Bear's diagnosis of mental insanity and the jury agreed that Hinckley was mentally incapable of understanding the crimes he had committed.[50]

In 1991, while engaged in a heated argument, Herbert Weinstein strangled his wife Barbara and then tried to cover the murder up by throwing her body from the window. Before the trial began, and because he had no history of violent behavior, Weinstein had an MRI followed up with a PET scan. Exams revealed an anomaly in Weinstein's prefrontal cortex and an arachnoid cyst growing in his left frontal lobe. These findings showed how the defendant was not able to control his aggressive behavior in a very stressful situation and thus he was found not criminally responsible due to mental defect.[51]

On October 18, 1992, Johnny Hoskins was arrested for having raped, beaten and strangled Dorothy Berger, an 80-year-old who lived in Brevard County, Florida. He was sentenced to death on April 4, 1994. Seven months later, Hoskins filed a Direct Appeal with the Florida Supreme Court (FSC), claiming that the trial judge had improperly barred neurological testing. Upon review, the FSC affirmed Hoskins's convictions, but remanded him to the State Circuit Court for a PET scan. Results showed Hoskins as having frontal lobe lesions and thus a lack of control of his inhibition restraints. Consequently, the FSC vacated the death sentence.[52]

In March 2010, Brian Dugan was admitted to Northwestern Memorial Hospital in Chicago to have an fMRI and a series of cognitive, attention and moral decision-making tests. In 1983, Dugan had kidnapped, raped, and beaten to death 10-year-old Jeanine Nicarico. One year later, he raped a 27-year-old nurse and drowned her in a quarry. In 1985, he kidnapped, raped, and killed a 7-year-old girl. The neuroscientist Kent Kiehl who concluded that Dugan's brain suffered from an anomaly in his prefrontal cortex performed neurological testing. Consequently, Dugan was incapable of controlling his impulses, differentiating right from wrong, and understanding the consequences of his actions. Kiehl's report was used to mitigate death penalty charges against Dugan.[53]

One recent study reported over 1585 cases between 2012 and 2015 in which neuroscience and behavioral genetics were reported in a judicial decision in the US criminal justice system. The data collected show an increasing use of neurological testing by the courts, with over 300 decisions in 2012 alone. Neurobiological evidence has been introduced in 5-6% of all murder trials and the most common type of brain scanning is MRI or CAT, rather than fMRI or SPECT. The study then highlights the use of neuropsychological testing and neuroimaging in pretrial proceedings as an improvement in the evaluation of subjective competency.[54]

Italian criminal trials - The Bayout case

In 2007, a forty-year-old Algerian, Bayout was involved in a quarrel in Udine, which erupted into a fight as the defendant usually wore eye make-up for religious reasons and for having been insulted with racial slurs. This led to his stabbing to death the individual who had provoked him. Sentenced to nine years in prison, the Court of Appeal made arrangements for a genetic test in which anomalies were detected in five of the genes linked to violent behavior, including a gene polymorphism (MAO-A). The court of justice stated that being a carrier of the low-activity allele for the MAOA gene (MAOA-L) would make Bayout more inclined to manifesting impulsive, aggressive behavior when provoked or socially excluded (from judgment no. 5-09/18/2009). Namely, he was affected by a kind of "genetic vulnerability" and the presence in the defendant's chromosomal inheritance of certain genes made him "particularly reactive in terms of aggressivity in stressful situations, and even more so if the individual had spent his childhood in a disadvantageous, family environment" (from sentence no. 5-09/18/2009). For these reasons, the Trieste Court of Justice reduced the sentence by one-third (Trieste (Italy) Court of Assizes Appeal no. 5 09/18/2009).

The Albertani case

The judge for preliminary investigations at the Como Criminal Court sentenced to twenty years in prison a young woman accused and found guilty of killing her forty-year-old sister. Besides also strangling her mother to death, she had tried to destroy the corpse by burning it. Simultaneous to the sentence being pronounced, a partial mental defect of the killer came to the judge's attention because of the results of specific neuroscientific tests intended to ascertain whether the woman presented those alleles significantly associated "with an increased risk of impulsive, aggressive and violent behavior" (from judgment 05/05/2011 no. 536). During the trial, the judge established the presence, through biological testing, of some unfavorable alleles present in the defendant's genetic inheritance, such as the low-activity MAO-A allele, SCL6A4 (STin2 polymorphism) and COMT (rs4680 polymorphism), with the sentence later essentially being reduced. High-resolution brain-imaging techniques (Voxel-based morphometry), were also used in the Como case, which proved how it was possible to make a definite correlation between anomalies in certain sensitive areas of the brain and the young murderer's antisocial actions, particularly, in the woman's brain where abnormally dense gray matter was found in the anterior cingulate. As a matter of fact, the test showed that the volume of gray matter mentioned above, in the anterior cingulate gyrus, turned out to be different from that in a control group of ten healthy women. It is noted that the previously mentioned cerebellar anatomical region is intended to inhibit automatic and instinctive behaviors. Moreover, in critical situations, it regulates aggressive reactions as well as mendacity (Como (Italy) Court, judgment 05/05/2011 no. 536).[55]

RESULTS AND DISCUSSION

If we further examine the risks listed by NASA for the space voyages completed so far, it seems incontrovertible to state that all kinds of possible emergencies can indeed take place in space. Some of these contingencies are known, while others are currently unknown. Indeed, the high degree of stress to which the astronauts could find themselves subjected could promote the gradual development of uncontainable stress in individuals whose genetic makeup contains particular polymorphisms or structural abnormalities in the brain that could lead an antisocial behavior being manifested. The protocol presented here is based on forensic neuroradiology and will have to be implemented together with the psychological and aptitude tests that are usually used in astronaut selection. Therefore it should consider, for maximum crew safety the genetic profile and brain anatomy of the candidates and in particular: 1) an examination of those brain structures involved in controlling aggressive impulses and possible anatomical malformations including the telencephalon and cerebral cortex on which the limbic system is present; 2) a study of some alleles that enable understanding the relationship between genetics and crime. In fact, the protocol should be based on examining those brain structures involved in controlling aggressive impulses and any anatomical defects inherent in the telencephalon in which the limbic system is present. Examinations must also be performed on the hypothalamic-pituitary-adrenal axis, (involved in the control and adaptation to stress) as well as on the connections between the limbic system (the seat of emotions) and the prefrontal cortex (control over impulses including aggressive ones) by using chemical imaging such as functional neuroimaging techniques that study brain function based primarily on measuring blood flow (fMRI), (SPECT), and glucose metabolism (PET) in different areas of the brain. Voxel-based morphometry (VBM) shows anatomical connections in the brain as well as the density of gray matter composed of neurons and of white matter that instead forms axons. Using this technique, anomalous structures in the brain can be highlighted – something that proved valuable in the Como court case discussed here.

The protocol then focuses on examining some of the biomarkers genetically predictive of criminal behavior. For example, regarding the polymorphisms mentioned here, the aspiring astronaut will have to have evaluated and monitored the monoaminergic system to determine the presence of the shorter MAO-A variant (on the X chromosome) in the polymorphic version of MAOA-L as well as the catechol O-methyltransferase (COMT) to confirm the Val158met polymorphism in the COMT. Regarding the serotonergic system, the SCL6A4 gene must be monitored as it is able to reduce aggressive behavior in humans that codes for the serotonin transporter (SERT), a key modulator of serotonergic transmission. The possible detection of reduced serotonergic activity in the brain may result in increased impulsive and aggressive behaviors via the "s" polymorphism of the SCL6A4 gene, whose existence involves a greater inability to adapt in unfavorable environmental conditions. The dopaminergic system will also be subject to careful study as, for example, the SLC6A3 gene (dopamine transporter) has been linked to extremely violent impulsive-aggressive and antisocial behaviors in an individual whose SLC6A3 gene is found to have the 10 allele.

CONCLUSIONS

The ability to image the interior of the human body with techniques with chemical imaging has revolutionized medical diagnosis and treatment. Clearly it appears evident that chemical imaging, forensic neuroradiology and behavioral genetics are able to produce innovations and undoubted benefits to the delicate task of understanding an individual's true personality. In fact, this research was able to show the validity of the application of chemical imaging to such an unusual forensic research field as that of space exploration.

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