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# Neural Plasticity in Space-Related Neuropsychiatric Disease and Injury: A Review

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**ABSTRACT:** Next-generation space medical advancements are presently driven by increased government and industry initiatives to plan and deliver feasible manned near-to-deep solar system exploration and habitation during the coming decades. The use of advanced precision medical techniques, such as brain stimulation, offers effective clinical and field/flight situation methods to selectively control vagal tone and neuroendocrine-modulated corticolimbic plasticity, which are impacted by prolonged cosmic radiation exposure, social isolation or crowding, and weightlessness in constrained operational non-terran locales. Earth-based clinical research shows that brain stimulation techniques can be used in conjunction with cutting-edge psychotherapeutic integrated memory structure theories to improve neuropsychiatric patient outcomes by corrective reconsolidation of arousing or emotional experiences, autobiographical memories, semantic schema, and other cognitive structures. These clever cotherapies or countermeasures, which take advantage of naturally occurring, pharmaceutically induced, and minimally invasive nervous system activity, may optimise the cognitive-emotional restructuring of astronauts suffering from space-related neuropsychiatric disease and injury, including mood, affect, and anxiety symptoms of any potential severity and pathophysiology. Deeper understanding of the illness states experienced by astronauts can be gained by appreciating improved neuropsychiatric healthcare through the fusion of new or rediscovered smart theragnostic medical technologies, capable of providing individualised neuroplasticity training and managed psychotherapeutic treatment protocols. Future research in this field should place a strong emphasis on the moral obligations of telemedicine and/or digital clinicians to advance (semi-)autonomous, technology-assisted medical prophylaxis, diagnosis, treatment, monitoring, and compliance of astronauts for improved health, safety, and performance in remote extreme space and extraterrestrial environments.

**KEYWORDS:** Astronaut Health, Cognitive-Emotional Reorganisation, Corticolimbic Plasticity, Neuropsychiatric Illness And Injury, Advanced Medical Technology, And Space Therapeutics

## I. INTRODUCTION

To start and finish even routine daily mission tasks and housing requirements in extraterrestrial conditions effectively, spaceflight-engaged astronauts frequently must execute with sustained high levels of physical, mental, emotional, and social competency. Stress brought on by prolonged exposure to severe environments, such as high-dose cosmic radiation, microgravity, and social isolation or crowding in small working spaces, increases hazards to astronauts' health, safety, and welfare and complicates already difficult mission objectives. In order to advance NASA's objectives for manned near-to-deep solar system exploration, the 2020 National Aeronautics and Space Administration (NASA) Technology Taxonomy roadmap continues to emphasise the importance of research and development into, and the application of, technologies and methods that improve human health, life support, and habitation in space and

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extraterrestrial environments. Medical diagnosis and prognosis, preventive and defence, behavioural health and performance, contactless and wearable human health and performance monitoring, long-duration health, and system transformational health and performance ideas are only a few of the specific areas of interest. These areas of focus are examined here in the context of neuropsychiatric insults, such as mood, affect, anxiety, personality, and psychotic problems [1–10], since spaceflight, gateway, and non-terran satellite/planetary surface circumstances change astronauts' neurobiology and psychology. It is thought that clever theragnostic cognitive-emotional restructuring can be used to reduce the detrimental impact that space exposure has on an astronaut's performance and mental health. Analog and real space investigations must be carried out to confirm the acceptability and efficacy of these kinds of therapies as plans for more short- to long-duration commercial space events, such as the recent SpaceX civilian Inspiration4 mission, and joint government-industry events, such as those of NASA's Artemis programme, continue to advance. For instance, the Artemis programme aims to land the second man and the first woman on the Moon from a lunar orbit Gateway over the course of the next ten years, establish a sustained human presence on the Moon by 2028, and further develop technologies, capabilities, and business plans for upcoming successful crewed spaceflight missions to Mars and other locations. The dangers involved with these tasks need more focus on the mental health of astronauts as well as the development and use of new techniques for monitoring, diagnosing, and treating medical emergencies in isolated space settings. In space travel and habitation, emotions and the arousing sensations that go along with them can weaken or strengthen the storage and retrieval of human memories, depending on the degree of intensity and associativity to autobiographical episodes and declarative knowledge. This has an impact on cognitive, social, and physical performance. Extreme emotional events and the memories that follow from them may also become maladaptive, leading to neuropsychiatric issues whether they vividly enter or stay inaccessible to human awareness, making astronauts susceptible to poor mental health outcomes in extraterrestrial environments. Lane et al. [11] and other professionals (such as [12,13]) have compiled appealing, albeit somewhat preliminary, psychotherapeutic strategies that (Earth) clinicians are now further researching. These strategies rely on carefully choosing which integrated memory structures of patients to reconsolidate. Clinicians will be better able to recognise and treat mood, affect, and anxiety disorders as well as the effects of traumatic brain injury with the help of these modified cognitive structures, which include (implicit/explicit) emotional responses, autobiographical memories, semantic schema, and other cognitive structures. Some of these programmes aim to use the Yerkes-Dodson law of arousal-modulated performance within (mental/physical) situational contexts to (1) recover or uncover patient memories of emotional traumas and (2) associate and then reconsolidate corrective cognitive representations and emotional responses with the same target memories through the appropriate use of a single single. The notion in its current form is plagued by methodological imprecision for Earth-based clinical effectiveness and compliance, despite the fact that this sort of methodology is inspired by well-established clinical and fundamental neuroscience research findings on memory modulation [14-24]. Such issues are prevalent in other purely psychotherapy approaches, and integrated memory structure rationales may only achieve the maximum clinical results in individuals with mild to moderate neuropsychiatric symptoms, even after revision. Situational challenges in locating and providing astronauts with neuropsychiatric diagnostic and treatment options further complicate issues for clinical success. Psychotherapeutic approaches may be appropriately optimised with the co-application of repurposed, newly emerging, and next-generation smart computer-interfaced theragnostic medical devices linked to assistive telemedicine technologies and medical social robot or virtual digibot therapists to overcome such gaps in medical prophylaxis, diagnosis, treatment, monitoring, and compliance. The prognosis for astronauts' mental health in alien conditions, such as space, as well as on Earth after their return will probably be improved by trends in cutting-edge therapeutics. Benefits from these improved theragnostic strategies may also be used to support innovative changes in health care for civilian populations on Earth who are exposed to growing challenges (such as extreme Earth environments, longer human lifespans, denser human populations and overcrowding, increased human desocialization or conflict, etc.), which may worsen mental health in a demographic group-dependent and/or -independent manner. Successes in translational medicine in the past, like NASA's involvement in bringing telemedicine to Earth-based medicine and underserved communities, may serve as models to change current trends in these fields, leading to more affordable, accessible, and efficient Earth medical policies and practises.

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## II. CHALLENGES RELATED TO COGNITIVE-EMOTIONAL RECONSTRUCTION

Physical activity, mental stimulation, and social support are common remedies for poor astronaut mental health. More study is required to understand how non-terran settings can affect the safety and efficacy of such therapeutic approaches, although neurotechnology and other- apy alternatives created for Earthlings may still apply to space travellers. Alternative neuropsychiatric techniques (as mentioned above) ignore how ground and flight physicians or coming smart medical social robots (cf. [25,26]) can produce treatment effectiveness that is closer to ideal. The Paro, eBear, Kaspar, Nao, and RoboTherapy companion robots as well as the Tess, Sara, Wysa, and Woebot digibots are current examples of inexpensive, accessible digital gadgets with strong therapeutic potential. These interactive meta-learning inferential devices, which communicate with patients via interpretable speech and text, offer sound remote (semi)autonomous smart assistive substitute healthcare solutions for patients who are experiencing symptoms of social isolation and stress, which are comparable to those related to the work and living conditions of space missions. They can be more successful, yet many psychotherapy techniques have not yet been tested on them. One key tactic is to combine the benefits of minimally invasive smart neuroprosthetic technologies, such as (1) vagus nerve stimulation (VNS), (2) transcranial electrical stimulation (TES), (3) transcranial near-infrared stimulation (TIRS), (4) transcranial magnetic stimulation (TMS), and (5) emerging smart pharmaceuticals, such as microRNA-targeting mimics, antagomirs, and antagonists, with digitally delivered psychotherapy and integrated memory structure rationales. For the treatment of mood, affective, and anxiety disorders that are currently resistant to traditional medication treatments and/or psychotherapy methods, several of these smart medical technologies are now commercially accessible or in the process of being developed. The frequently labile, progressive, and irreversible expression of forebrain pathophysiologies in some of the most severe mental illnesses makes patients refractory to otherwise well-known, safe (and bearable), disease prophylaxes, management, and therapies. Even patient populations on Earth with mild to severe psychiatric diseases, such as chronic depression and tier-specific post-traumatic stress disorder, react to psychotherapy, chemotherapy, or combination psychotherapy/chemotherapy with considerable rates of chronic and acute symptom recurrence [40,41]. For patients displaying complex emotional components, integrated memory structure rationales aim to enhance the efficacy of regular psychotherapy, especially since it reduces the problematic heterogeneity of psychotherapy choice and delivery (e.g., poor psychotherapeutic entry points, client-clinician rapport, patient compliance, trauma identification and schema restructuring, etc. However, a lot of doctors who endorse the rationales for integrated memory structures noticeably omit to specify how to establish and maintain appropriate, therapeutic (i.e., moderate) levels of patient arousal in therapeutic settings. Additionally, they frequently fail to properly take into account illnesses for which these programmes may only have limited effectiveness, such as cognitive-behavioral deficits coupled with substantial persisting anatomical and functional abnormalities in the corticolimbic system.

## III. ADANCED SOLUTION OF CHALLENGES

In both theory and practise, the process of reforming and reactivating memories in order to achieve cognitive-emotional restructuring in patients necessitates extremely regulated physiological conditions of either healthy or (remedied) diseased nerve systems. Modern smart precision medicine may give space medicine practitioners the crucial clinical tools they need to fix these problems by using integrated memory structure justifications and, as a result, boost their therapeutic potential. Smart neuroprosthetics and drug delivery systems can be used to treat many neuropathologies seen in the hippocampus, amygdala, medial prefrontal, and cingulate cortices (cf. [14,28,32,33,42-45]) by acting via highly selective substrate and temporal targeting of disease-affiliated molecules, cellular organelles and pathways, brain networks, and nerve fibre groups. These pathologies relate to mood, affective, and anxiety disorders as well as hypoxic and ischemic brain damage, and include, among other things, (1) disturbances in neuro- and synaptogenesis, (2) protein expression, (3) neuronal excitotoxicity and glial proliferation, and (4) glucocorticoid-dependent neu-rotrophic factor concentrations. Through focused neuroplasticity training, these cutting-edge technologies not only compensate for coexisting neurological conditions but also successfully change patient learning, memory, and executive function (e.g., [14,15,31,46-48]). The signal-to-noise ratio of neurotransmission (e.g., [14,53]), brain synaptic plasticity (e.g., [14,44,45,49,50]), single-unit and field potential phasic activity (e.g., [14,51,52]), and neurotransmitter synthesis, release, and re-uptake (e.g., [14,54,55]) are all altered by targeted neuroplasticity training.

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## IV. TMS AND COGNITIVE-EMOTIONAL RECONSTRUCTION

The more or less direct biological link between the production and recall of traumatic emotional experiences makes the use of VNS to promote cognitive-emotional reorganisation in astronauts appealing. By directly enhancing or imitating neural communication and the (structural and functional) connectivity between the limbic and cortical areas, TMS, another potentially effective treatment adjuvant, may also help patients with cognitive-emotional restructuring, assisting with memory consolidation and retrieval (cf. [83–88]). Since TMS avoids enlisting the vagal system, it should be assumed that the corticolimbic plasticity caused by precise TMS alone is less reflective of the biological processes and brain alterations that normally follow emotional events than VNS. TMS has nevertheless been demonstrated to be a reliable method for altering the accuracy and storage capacity, retrieval, and/or reconsolidation of emotional memories in animal models of anxiety, as well as in people who have experienced emotional trauma in real life or who are subjected to artificially induced emotional situations (e.g., [89–94]). TMS has shown impressive success in modifying memory characteristics and performance levels that are specific to a patient's sensorial/perceptual modalities, gender, degree of attention, and emotional, semantic, and procedural content of patient memories [95–101]. This has encouraged its use in the treatment of a variety of psychiatric conditions, including schizophrenia, major depression, dementia, post-traumatic stress disorder, and other psychiatric disorders (e.g., [102–109]). Though the targeted phenomenological effects of TMS on patients' memory and cognition, and consequently their psychiatric status, are largely the result of physiological tuning and the reorganisation of lower-band brain function, frequently through large-scale network interference or facilitation (cf. [109-114]), the cytological and biochemical mechanisms mediating such plasticity are only now being clarified. According to preliminary sets of findings, TMS alters synaptic transmission, as well as corresponding synaptic structure and density, in a manner that is intensity-specific, similar to VNS, and that these changes are caused by altered brain concentrations of (1) amino acid and bioamine neurotransmitters, (2) neurotrophic factors, and (3) protein kinase-dependent kinase-dependent protein synthesis, transcription, and cell metabolism and growth [115–120]. Together, these and other data suggest that the use of TMS in conjunction with psychotherapeutic techniques offers a secure, effective means of achieving cognitive-emotional reorganisation in Earth patients (e.g., [121]), and maybe astronauts.

## V. FUTURE ASPECTS

The use of cutting-edge smart precision medicine will inevitably improve psychotherapeutic integrated memory structure rationales for the corrective reconsolidation of traumatic arousing or emotional experiences, autobiographical memories, and semantic schema. With the aid of neuroprosthesis-driven VNS or TMS, for instance, physicians may use these justifications to target specific vagal tone and psychiatric trauma-related brain processes for a more individualised, effective, noninvasive approach to treating mood, affective, and anxiety disorders. Existing neurotechnologies can be quickly and affordably adapted for use in space medicine without adding significant weight to the payload or placing a significant burden on the health, life support, or habitation systems. Instead, choices among commercially available small portable stimulation and wearable monitoring devices made for Earth-based clinical treatment of various neuropsychiatric and motor indications are available. These kinds of devices may be fitted with minimally invasive contact or contactless sensor/stimulator-connected computer interfaces, which can be programmed with user-friendly proprietary software, even though legal, regulatory, and ethical issues still exist for Earth medical policies and practises (e.g., [25,26,122,123]). To diagnose, treat, and monitor patients based on a variety of smart real-time biomarker data analytics and electronic record keeping (e.g., [59,124-127]), these systems may also be linked with (ultraparanoid computing) encrypted semi-autonomous or autonomous mobile or stationary virtual re- mote medicine systems. These systems may include, but are not limited to, those associated with typical physiological vital signs, brain function, and continuous body fluid chemical profiles. Although these benefits of space deployment, psychotherapy techniques require clinician-completed patient evaluations, such as semi-structured and structured inventories that are standardised in the industry, and clinician-led treatment sessions in order to maximise patient outcomes. Neurotechnologies must smoothly and cooperatively integrate clever human-emulating social medical robots or virtual digibot therapists to carry out interactive psychotherapy in conjunction with the operation of neuro-cybernetic prosthetic systems in the absence of human clinical practitioners. Artificially intelligent, deep-learning, and meta-learning inferential digital therapists have undergone extensive development over many decades. This work has had a variety of positive effects on patient populations, from paediatric to geriatric cohorts, in terms of their mental health and wellbeing (e.g., [25,26,122,123]). These technologies are shown by successful results recorded for the previously

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covered social robots and digibots [122], which may be telemedically connected via neurocybernetic prosthetic command and control systems for optimum VNS or TMS administration. To improve patient outcomes both on Earth and in environments beyond Earth, research and development must focus on enhancing the safety, efficacy, and clinician-patient relationship of digital therapists. Despite this, progress in this field is still modest. The use of more potent, internally and externally valid, precise psychological, biological, behavioural, and digital biomarkers as well as more dependable and accurate fast theragnostic computational models that better manage data workloads/-flows for better patient therapy experiences as well as personalised mental health diagnosis and monitoring are some current observable gaps in the state-of-the-art systems. While promising computational model examples include feature classifier/extraction/prediction algorithms capable of adaptive quasi-model-free/-based neural net embedding, trainable distributed cognition-emotion mapping, and artificial (surrogate th)earing, promising disease marker examples include constellations incorporating acoustic, structural, and semantic language production, use, and comprehension to detect the onset and severity of neuropsychiatric conditions [128-134]. Many of these artificial intelligence and machine learning milestones are still being stressed in the competitive biotechnology and medical commercial sectors based on Earth, and they could realistically be accomplished over the next five to eight years with safe, effective deployment for suitable space and extraterrestrial utility within the decade [134].

## VI. CONCLUSION

In the coming ten years, committed research and development by the private sector, the public sector, and academia will significantly advance these emerging technologies and their clinical application, including the successful integration of artificial surrogate-mediated therapeutic approaches with intelligent interoperable pharmaceutical and other treatment delivery systems [1,133]. This future requires appropriate government and business control of technological efficacy, privacy, and security. The seamless, high-quality deployment of intelligent artificial surrogate clinicians for both Earth and space medicine objectives depends on rigorous, transparent dialogue regarding appropriate technology-assisted medical information storage and utilisation. Such extensive, well-coordinated community activities promote cultural comprehension of the benefits of intelligent technologies, both medically and economically, and the societal role they play. They also encourage and maintain consumer confidence and good patient-provider relationships. In order to decide if and which artificially intelligent surrogate clinician technologies should be subject to standard healthcare technology regulatory examination and approval, more precise, enforceable rules [25,26,121-123,132-135] must be developed. The establishment of best policies and practises for educating healthcare providers on the use of technology in various healthcare models, professional organisation recommendations, satisfying duties of care, reporting harm, and providing reliable pathways for risk assessment and service referral are just a few topics that guidelines may cover. Transparency in technology supervision and services that respect patient autonomy, vulnerability, and privacy, the examination and mitigation of institutionalised and personal biases that result in unwelcome disparities in the delivery of technology and services; and A few examples of inequities are (1) the state of diagnostic validation, (2) the availability of free platforms for obtaining and sharing digital biomarker data, (3) the suitability of behavioural and digital phenotyping, (4) the depth of data-driven learning engines, (5) the use of real-world evidence, (6) the expense and infrastructure for data storage and analysis, (g) seamless data integration with clinical records, and (7) policed data ownership and protection.

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