Topical: Smart Theragnostic Cognitive-Emotional Restructuring for Space-Related Neuropsychiatric Disease and Injury

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Abstract

Application of cutting-edge smart precision medicine, in combination with new psychotherapeutic integrated-memory-structure rationales for corrective reconsolidation of arousing or emotional experiences, autobiographical memories, semantic schema, and other cognitive structures, provides powerful clinical and field/flight-situation methods to selectively modify vagal tone and corticolimbic plasticity. Such cotherapies, which exploit both natural and smart neuroprosthesis-driven nervous system activity, may optimize 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. Appreciation of improved neuropsychiatric healthcare through the integration of emerging new or rediscovered theragnostic medical technologies with adaptable psychotherapeutic treatment protocols will reveal both deeper insights about illness states experienced by astronauts and necessary research and development directions to further advance technology-assisted neuroplasticity training for astronaut health, wellbeing, and performance in space and extraterrestrial environments.

1. Introduction

Spaceflight-engaged astronauts must often perform with sustained high physical, mental, emotional, and social proficiency to satisfactorily begin and complete even routine daily mission duties and habitation needs in nonterrestrial environments. Stresses caused by constant extreme-environment exposure, such as high-dose cosmic radiation, microgavity, and social isolation or crowding in confined operational locations, exacerbate risks to the health, safety, and wellbeing of astronauts and further jeopardize already challenging mission goals and outcomes. Expectedly, the 2020 National Aeronautics and Space Administration (NASA) Technology Taxonomy roadmap continues to underscore the need for research, development, and application of technologies and methods that improve human health, life support, and habitation in space and extraterrestrial environments in furtherance of NASA's goals for manned near-to-deep solar system exploration. Specific areas of interest include, among other categories, medical diagnosis and prognosis, prevention and countermeasures, behavioral health and performance, contactless and wearable human health and performance monitoring, long-duration health, and system transformative health and performance concepts. These areas of emphasis are surveyed here in the context of neuropsychiatric insult, such as mood, affect, anxiety, personality, and psychosis disorders [1-10], due to modifications in astronaut neurobiology and psychology associated with spaceflight, gateway, and nonterran satellite/planetary surface conditions. In particular, smart theragnostic cognitive-emotional restructuring is considered as a means to mitigate negative space-induced effects on astronaut mental health, wellbeing, and performance.

Emotions and the arousing sensations accompanying emotions can weaken or strengthen the storage and retrieval of human memories, impacting cognitive, social, and physical performance in relation to the level of intensity and associativity to autobiographical episodes and declarative knowledge. Moreover, extreme emotional experiences and resultant memories may become maladaptive, causing neuropsychiatric problems whether they vividly enter or remain inaccessible to human consciousness. Lane et al. [11] and other experts [e.g., 12, 13] have synthesized appealing, albeit somewhat preliminary, psychotherapeutic programs now being further investigated by clinicians that rely on selectively reconsolidating patient integrated-memory structures, comprised of (implicit/explicit) emotional responses, autobiographical memories, semantic schema, and other cognitive structures, to better understand and treat mood, affect, and anxiety disorders. Some of these programs, which may render good prevention, intervention, and postvention techniques for astronaut mental health, aim to apply 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) to associate and then reconsolidate corrective cognitive representations and emotional responses with the same target memories through appropriate use of a single psychotherapeutic modality or various modality combinations (i.e., behavioral, cognitive-behavioral, emotion-focused and/or psychodynamic/psychoanalysis approaches). While this type of technique is inspired by well-established clinical and basic neuroscience research findings on memory modulation [14-24], the concept in its present form is beset by methodological imprecision for Earth-based clinical efficacy and compliance, as is common in other purely psychotherapeutic strategies, and it might only find, even after revision, the greatest clinical success in patients presenting medically tractable mild to moderate neuropsychiatric symptoms. These problems are exacerbated by situational difficulties in finding and administering neuropsychiatric diagnosis and treatment solutions to astronauts. To overcome such gaps in medical prophylaxis, diagnosis, treatment, monitoring, and compliance, psychotherapeutic approaches may be suitably optimized with 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. Such trends in state-of-art theragnostics will benefit astronaut mental health prognosis in space and extraterrestrial environments as well as terran environments following the return of astronauts to Earth.

2. The Problem of Optimal Cognitive-Emotional Restructuring

Typical countermeasures for poor astronaut mental health involve physical exercise, cognitive recreation, and social-emotional supports. However, neurotechnology and cotherapy alternatives developed for Earth inhabitants may extend to space travelers. Alternative neuropsychiatric approaches noted above neglect how ground and flight clinicians or emerging smart medical social robots or digibots [cf. 25, 26] can achieve closer to optimal therapeutic efficacy by incorporating psychotherapy and integrated-memory structure rationales with advantages offered by minimally invasive smart neuroprosthetic technologies, such as vagus nerve stimulation (VNS) transcranial electrical stimulation (TES), transcranial near infrared stimulation (TIRS), transcranial magnetic stimulation (TMS), and emerging smart pharmaceuticals, such as microRNA-targeting mimics, antagomirs, and micro-/nanosized drug-delivery, regenerative, and surgical platforms [27-39]. Many of these smart medical technologies are either already commercially available or undergoing reduction-to-practice for the control of mood, affect, and anxiety disorders currently resistant to conventional drug and/or psychotherapeutic techniques. In some of the most severe psychiatric conditions, oftentimes labile, progressive, and irreversible expression of forebrain pathophysiologies render patients unresponsive to otherwise known safe (and tolerable) disease prophylaxes, management, and treatments. Even Earth patient populations suffering from mild to moderate psychiatric disorders, such as tiered posttraumatic stress disorders and chronic depression, respond to psychotherapy, chemotherapy, or joint psychotherapy/chemotherapy with significant chronic and acute symptom relapse rates [40, 41]. Integrated-memory-structure rationales seek to improve upon the effectiveness of standard psychotherapy for patients showing complex emotional components, especially as it limits problematic heterogeneity of psychotherapy choice and administration (e.g., poor psychotherapeutic entry points, client-clinician rapport, patient compliance, trauma identification and schema restructuring, etc.). Yet many clinicians in support of integrated-memory structure rationales notably fail to detail methods for determining and eliciting suitable, consistent therapeutic (i.e., moderate) levels of patient arousal in therapeutic environments and to fully account for diagnoses for which these programs may yield less than marginal efficacy, such as cognitive-behavioral impairments accompanied by serious persistent corticolimbic structural and functional abnormalities.

3. Smart Solutions for the Problem of Optimal Cognitive-Emotional Restructuring

The process of reactivating and reforming memories to accomplish cognitive-emotional restructuring in patients demands, in theory and practice, very controlled physiological states of healthy or (remedied) afflicted nervous systems. Cutting-edge smart precision medicine may provide space medicine practitioners with much needed clinical tools to resolve such flaws in implementting integrated-memory-structure rationales and, therefore, to increase their therapeutic potential. Smart neuroprosthetics and drug-delivery systems, acting via highly selective substrate- and temporal-targeting of disease-affiliated molecules, cellular organelles and pathways, brain networks, and nerve-fiber groups, can be employed to overcome many neuropathologies observed in the hippocampus, amygdala, and medial prefrontal and cingulate cortices [cf. 14, 28, 32, 33, 42-45]. Such pathologies include, among other changes, disturbances in neuro- and synaptogenesis, protein expression, neuronal excitotoxicity and glial proliferation, and glucocorticoid-dependent neurotrophic factor concentrations, which are connected to mood, affect, and anxiety disorders. Besides compensating comorbid neurological states, these advanced technologies also effectively alter patient learning, memory, and executive function [e.g., 14, 15, 31, 46-48] through targeted neuroplasticity training which modulates brain synaptic plasticity [e.g., 14, 44, 45, 49, 50], single-unit and field-potential phasic activity [e.g., 14, 51, 52], signal-to-noise ratio of neurotransmission [e.g., 14, 53], and neurotransmitter synthesis, release, and re-uptake [e.g., 14, 54, 55].

4. Cognitive-Emotional Restructuring via Vagus Nerve Stimulation

In the case of VNS, which mimics viscerosensory information associated with emotional events and arousal critical to integrated-memory-structure rationales, corticolimbic plasticity is generated from titrated, feedback-controlled stimulation parameters that fall well below the threshold for maximal activation of unmyelinated vagal C fibers. Although the vagus nerve is comprised of myelinated and unmyelinated afferents, subthreshold stimulation parameters produce moderately arousing (implicit/explicit) cardiopulmonary neural signals that are carried by myelinated afferents to the brain. Such signals exert widespread polysynaptic control over brain function and behavior [cf. 55], including replicating the Yerkes-Dodson inverted-U-pattern of memory modulated performance in humans and animals [14, 15, 46, 47]. Memory performance changes correlate with respective protracted increments and decrements in hippocampus and medial prefrontal cortex pyramidal cell responses characteristic of bioamine-dependent long-term potentiation and depression [14, 49, 50]. Further VNS-induced plasticity manifests in beta- [46, 51], theta- [cf. 14, 56], and gamma-band [14, 52] spectral power alterations in corticolimbic field potentials thought essential for encoding, consolidating, retrieving, and reconsolidating autobiographical emotional information and semantic schema. While these VNS findings are largely taken from protocols typically delivered through surgically implanted programmable devices, similar results are predicted for protocols delivered through more noninvasive transcutaneous electrical and magnetic nerve stimulation [cf. 57, 58]. Optimal technological feasibility and effectiveness of these and other newer minimally invasive techniques in Earth and in space and extraterrestrial environments depend on ongoing advances in wearable wireless nervous system-computer interfaces to automatically detect and initiate realtime responsive neurostimulation for psychiatric crises [cf. 59]. And, as with other precision medical technologies, their exact reproducible application surpasses the psychotherapeutic value of older alternative techniques, such as generating arousal from hand-held dynamometers, and may be paired, for instance, with emotion-laden content of (computer-presented) stimuli or additional methods to adjust disorder-compromised vagal tone. Astronauts experience vagal tone perturbation under physical and emotional stress and, therefore, are superb candidates for VNS-aided cognitive-emotional restructuring to remedy any possible mood, affect, and anxiety disease severity forced by microgravity and work conditions.

5. Cognitive-Emotional Restructuring via Transcranial Magnetic Stimulation

Use of VNS to enhance cognitive-emotional restructuring in astronauts is attractive for its more-or-less straightforward biological relationship to the formation and retrieval of traumatic emotional memories. TMS, another potentially efficacious treatment adjuvant, may also facilitate patient cognitive-emotional restructuring by directly improving or impairing neural communication and (structural and functional) connectivity between limbic and cortical areas contributing to memory consolidation and retrieval [cf. 60-65]. In comparison to VNS, corticolimbic plasticity induced by precise TMS alone should be considered less representative of naturally occurring bioprocesses and brain changes accompanying emotional experiences, since TMS bypasses recruitment of the vagal system. Nevertheless, TMS has been shown to be a credible means for modifying the storage capacity and accuracy, retrieval, and/or reconsolidation of emotional memories in animal models of anxiety and in humans suffering from real-life emotional traumas or enduring experimentally constructed emotional situations [e.g., 66-71]. The impressive successes of TMS for altering memory attributes and performance levels specific to patient sensorial/perceptual modalities, patient gender, degree of patient attention, and emotional, semantic, and procedural content of patient memories [72-78] has encouraged its application for the treatment of major depression, dementia, post-traumatic stress disorder, schizophrenia, and other psychiatric conditions [e.g., 79-86]. Though targeted phenomenological effects of TMS on patient memory and cognition, and therefore psychiatric status, largely result from physiological tuning and reorganization of lower-band brain function, often through large-scale network interference or facilitation [cf. 86-91], the cytological and biochemical mechanisms mediating such plasticity are only now being elucidated. Preliminary sets of findings indicate that TMS effects changes in synaptic transmission as well as corresponding synaptic structure and density in an intensity-specific manner, similar to VNS, and that such changes result from altered brain concentrations of amino acid and bioamine neurotransmitters, concentrations of neurotrophic factors, and protein-kinase-dependent protein synthesis, transcription, and cell metabolism and growth [92-97]. Taken together, these and additional findings indicate combined use of TMS with psychotherapeutic strategies provides a safe, efficacious way to effect cognitive-emotional restructuring in Earth patients [e.g., 98] and perhaps astronauts.

6. Nervous System-Computer Interfaces, Medical Robots or Digibots, and the Future of Seamless Integrated Device-Driven Theragnostic Cognitive-Emotional Restructuring

Psychotherapeutic integrated-memory-structure rationales for corrective reconsolidation of traumatic arousing or emotional experiences, autobiographical memories, and semantic schema are predictably enhanced by co-application of cutting-edge smart precision medicine. Combining these rationales with neuroprosthesis-driven VNS or TMS, for example, allows clinicians to selectively modify vagal tone and brain processes associated with psychiatric trauma for more personalized, optimal noninvasive treatment of mood, affect, and anxiety disorders. Choices among commercially available small portable stimulation and wearable monitoring devices designed for Earth-based clinical treatment of various neuropsychiatric and motor indications permits existing neurotechnologies to be expediently and cheaply adapted for space medicine purposes without incurring high payload and health, life support, and habitation systems burdens. Although legal, regulatory, and ethical issues remain for Earth medical policies and practices [e.g., 25, 26, 99. 100], these sorts of devices may be equipped with minimally invasive contact or contactless sensor/stimulator-connected computer interfaces which can be programmed with user-friendly proprietary software and may be linked with (ultraparanoid computing) encrypted semi-autonomous or autonomous mobile or stationary virtual remote medicine systems to diagnose, treat, and monitor patients based on a range of smart realtime biomarker data analytics and electronic record keeping [e.g., 59, 101-104], including, but not limited to, those associated with typical physiological vital signs, brain function, and continuous body-fluid chemical profiles.

Despite these space-deployment advantages, psychotherapeutic methods require clinician-completed patient assessments, such as industry-standardized semistructured and structured inventtories, and clinician-guided therapy sessions to maximize patient outcomes. In absence of human clinical practitioners, neurotechnologies must seamlessly and interoperably integrate smart human-emulating social medical robot or virtual digibot therapists to execute interactive psychotherapy in coordination with operation of neurocybernetic prosthetic systems. Considerable amounts of work over many decades continue to refine and improve artificially intelligent, deep- and meta-learning digital therapists, resulting in varying positive mental health and wellbeing impacts on patient populations from pediatric to geriatric cohorts [e.g., 25, 26, 99. 100]. That said, progress remains slow in this area and research and development need to concentrate on increasing safety, efficacy, and clinician-patient rapport of digital therapists for the best patient outcomes on Earth and in environments beyond Earth. Some current identifiable gaps in the state-of-art involve determining and using more powerful, internally and externally valid, and precise psychological, biological, behavioral, and digital biomarkers as well as more reliable and accurate fast theragnostic computational models that better manage data workloads/-flows for superior patient therapy experiences and personalized mental health diagnosis and monitoring. Promising disease-marker examples include constellations incorporating acoustic, structural, and semantic language production, use, and comprehension to detect onset and severity of neuropsychiatric conditions [105-109]. Whereas, promising computational model examples include feature classifier/extraction/prediction algorithms capable of adaptive quasimodel-free/-based neural net embedding, trainable distributed cognition-emotion mapping, and artificial personality trait parameterization for machine intuitive causal physics and psychology, compositionality and learning-to-learn, and efficient realtime gradient-descent deep learning and thinking [25, 110]. Many of these milestones continue to be emphasized in competitive Earth-based biomedicine/-technology commercial sectors and may be realistically achieved over the next five to eight years with safe, efficacious deployment for suitable space and extraterrestrial utility within the decade.

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