AI-Driven Virtual Reality Therapeutic Medicine for Patients with Cognitive Impairment: Increasing Neuroplasticity through Attention Exercises, Non-Player Character Engagement, and Brain-Motor Game Modulation

Anthony Faiola, PhD, MFA, MA, MA

Presentation Overview

Dr. Faiola's research lies at the intersection of digital health and medical virtual/extended reality, focusing on the development of three emerging health technologies: **(1)** AI-driven virtual reality therapeutic medicine (VRx), **(2)** Volatile organic compound (VOC) biomarker biosensors, and **(3)** Mobile health (mHealth). These digital health projects are funded by NIH, American Cancer Society, Merck, UC Cancer Center, the UC Gardner Neuroscience Institute, and the Indiana University Health and the IU Health Neuroscience Center. His presentation will review his current research in VRx and the impact of VR on cognitive impairment. He will discuss his current studies with neuro-oncology patients (UC), delirium patients (IU), dementia patients (UC), and stroke patients (Sapienza University, Rome, Italy). He will discuss the findings of a prior pilot study with brain cancer patients at the University of Kentucky. The title for that study/paper is: Investigating the Usability, Feasibility, and Effect of a Virtual Reality Cognitive Training System on Brain Cancer Patients with Mild Cognitive Impairment: A Quasi-Experimental (Single-Arm) Pilot Study. He will also discuss his VR cognitive rehabilitation training (VR-CRT) intervention, which provides the synergistic effects of selection attention training with immersive VR navigation, offering a unique mechanism of neurotransmitter stimulation. Based on this VRx platform he developed over the last seven years, he is currently running four consecutive clinical studies as noted above. He is also in an early partnership with colleagues at the Barrow Neurological Institute (Phoenix, AZ) in an integrated multimodal lifestyle intervention study that includes his VRx 2.0 AI-driven platform, plasma p-Tau217 biomarker testing, and physical activity and time restricted eating tracking.

Background

Cancer: Studies show that at the time of diagnosis for brain cancer (glioblastoma) patients (including 6 months following radiation and chemotherapy), 50%–80% of brain cancer patients report cognitive dysfunction, with some data showing cognitive impairment as high as 91%.[1] Within the glioma population, cognitive impairment ranks first among all concerns following treatment.[2, 3] Specifically, cancer-related cognitive impairment (CRCI) is prevalent in up to 75% of all cancer survivors, [4-6] being a persistent cognitive disability frequently experienced during or after treatment.[5, 7] One report states that 35% of cancer survivors continue to exhibit CRCI for months and years following treatment.[8] The devastating effects of CRCI [4, 9-12] affect working memory, attention, processing speed, and executive function as well as the disabling psychosocial effects of depression, anxiety, deterioration of social and family relations and work life.[5, 13, 14] Consequently, CRCI has a destructive impact social functioning and the health-related quality of life.[5, 15-17] CRCI has gained increasing recognition as a leading issue for BCS.[13] Statistical estimates suggest that by 2020 there were over 70 million cancer survivors (all types) worldwide, which highlights the global impact of cognitive impairment and why it is a significant concern for many health care professionals. [18-21]

Dementia: Research has demonstrated that functional brain network dysconnectivity in patients with early subclinical neurodegenerative disease, plays a major role in those with Alzheimer's disease and related dementia (AD/ADRD).[22, 23] Within this pathological framework, acute and chronic cognitive impairment result from widespread neural network dysfunction, disruption and neurotransmitter imbalances associated with brain injury. Affected areas include all cerebral lobes as well as subcortical areas, which researchers suggest impact the patients' large-scale distributed neural networks.[24, 25] Hence, dementia leads to reduced alertness and pronounced inattention, resulting in diffuse cognitive deficits, [26-28] including those distributed regions of the frontoparietal, cingulo-opercular, and salience networks.[29] Considerable clinical and scientific effort has been made to reduce mild cognitive impairment (MCI) for older adults, particularly for MCI/dementia. [30-32]

Stroke: Globally, there are approximately 93.8M people living with the aftereffects of a stroke. [33] Post-stroke mild cognitive impairment (PMCI) is defined as the occurrence of cognitive deterioration after stroke, ranging from minor impairment to dementia. [34, 35] Research has demonstrated that the prevalence of PMCI in the first year after stroke is 40%, with follow-up studies showing PMCI at 61% among 10-year survivors. [35, 36] This underscores the urgent need for scalable non-pharmacological interventions that leverage innovative technologies such as virtual reality (VR) to engage impaired brain circuity and promote attention/arousal in the middle cerebral artery territory—which supplies the cerebral cortex (specifically the frontal, parietal, and temporal lobes), i.e., those brain regions most frequently and severely affected by stroke. [37]

Prior Approaches: Great clinical and scientific effort has been applied to reduce cognitive impairment for patients suffering from cognitive impairment with mixed results. Prior approaches to address cognitive impairment include physical exercise, [38] mindfulness training,[39][40][41] crossword puzzles,[42][43] and cognitive digital stimulation techniques. [44-47]

Pharmacotherapeutic interventions have helped manage some cognitive symptoms but often with conflicting outcomes, [44, 46-51] and serious side-effects (e.g., nausea, vomiting, diarrhea, dizziness, and/or cardiac arrest). [52-59] In addition, there has been a considerable lack of cognitive rehabilitation services with scalability and reach for AD/ADRD patients. [60-62] As such, there is a strong need to develop innovative treatments for the AD/ADRD population that can offer an effective and sustainable recovery model to mitigate downstream MCI degeneration.

Virtual Reality Therapeutic Medicine

Virtual Reality is an interventional therapy ideally suited for in-home or clinic cognitive training that could overcome the limitations of current treatment of MCI.[63, 64] By leveraging VR's potential for producing immersive 3D visual stimuli for patients, we can effectively engage the frontoparietal network, involved in visuospatial memory and the salience network necessary for attention. [65, 66] While studies confirm that brain function networks are frequently disrupted in AD/ADRD patients,[67][68] VR training has shown to be effective in cognitive rehabilitation, impacting functional networks, such as the cortical visuospatial and attention areas.[69][70] A plethora of studies on the effects of VR on dementia patients with MCI[71-73] has demonstrated VR's potential as an effective cognitive assessment and therapeutic tool[74][75] for improving cognitive performance. Many of these VR studies utilize off-the-shelf or task-centered programs, while others offer a narrative approach, e.g. preparing a meal. We argue that early delivered non-invasive VR as a therapeutic intervention can engage impaired brain circuity and promote attention and arousal as a novel approach to managing the symptoms of cognitive impairment. Within a 3D immersive VR environment, cognition takes on the role of tagging memories with respect to context (location/time),[76] functioning as a reciprocal connection to the rest of the brain through the pathways of the neo/frontal cortex. Decades of research have demonstrated that spatial navigation, perception of time, and memory functions depend on regions of the medial temporal lobe that include the hippocampus and entorhinal corte.[77][78][79][80] By leveraging VR's potential for producing immersive 3D visual stimuli we can effectively engage the frontoparietal network, involved in visuospatial memory[81] and the salience network necessary for attention.[82] In sum, immersive VR experiences for cognitively impaired patients may aid in the organization of events in different relational cognitive maps that form episodic memory.[83][84]

Dr. Faiola's VRx platform uses several unique AI-driven technologies: 1) Immersive cognitive training exercises with predictive performance metrics, 2) Intelligent (AI agents) non-player characters (NPCs) that engage with patients using language sentiment analysis, where patient-directed brain health (PROMIS) questions provide real-time diagnostic cognitive data, along with large language models to create emotionally responsive, context-rich dialogues, 3) PEM and NPC modelling that adapt cognitive rehabilitation therapy by adjusting game difficulty based on performance, and 4) Brain games that combine physical exercise and motor cognitive tasks to improve patient brain plasticity, memory, and motor skills to maximize patient neurostimulation.

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