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Is Clinical Virtual Reality Ready for Primetime?

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Abstract

Objective: Since the mid-1990s, a significant scientific literature has evolved regarding the outcomes from the use of what we now refer to as Clinical Virtual Reality (VR). This use of VR simulation technology has produced encouraging results when applied to address cognitive, psychological, motor, and functional impairments across a wide range of clinical health conditions. This article addresses the question, "Is Clinical VR Ready for Primetime?" Method: After a brief description of the various forms of VR technology, we discuss the trajectory of Clinical VR over the last 20 years and summarize the basic assets that VR offers for creating clinical applications. The discussion then addresses the question of readiness in terms of the theoretical basis for Clinical VR assets, the research to date, the pragmatic factors regarding availability, usability, and costs of Clinical VR content/systems, and the ethical issues for the safe use of VR with clinical populations. Results: Our review of the theoretical underpinnings and research findings to date leads to the prediction that Clinical VR will have a significant impact on future research and practice. Pragmatic issues that can influence adoption across many areas of psychology also appear favorable, but professional guidelines will be needed to promote its safe and ethical use. **Conclusions:** While there is still much research needed to advance the science in this area, we strongly believe that Clinical VR applications will become indispensable tools in the toolbox of psychological researchers and practitioners and will only grow in relevance and popularity in the future. **Keywords:** Clinical Virtual Reality, Psychology, Rehabilitation, Neuropsychology

Public Significance Statement: Virtual Reality (VR) technology offers new opportunities for clinical research, assessment, and intervention. Advances in the underlying VR-enabling technologies and methods can now support the creation of low-cost, yet sophisticated, immersive and interactive VR systems, capable of running on consumer-level computing devices. It is predicted that the clinical use of VR will have a significant impact on mental healthcare in areas where the research demonstrates added value.

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Introduction

Virtual Reality (VR) technology offers new opportunities for clinical research, assessment, and intervention. Since the mid-1990s, VR-based testing, training, and treatment approaches have been developed by clinicians and researchers that would be difficult, if not impossible, to deliver using traditional methods. During this time, a large (but still maturing) scientific literature has evolved regarding the outcomes and effects from the use of what we now refer to as *Clinical VR* applications targeting cognitive, psychological, motor, and functional impairments across a wide range of clinical health conditions. Moreover, continuing advances in the underlying enabling technologies for creating and delivering VR applications have resulted in its widespread availability as a consumer product, sometimes at a very low cost. So, when one studies the scientific literature, examines the evolving state of the technology, and observes the growing enthusiasm for VR in the popular culture, a big question emerges for psychology, neuropsychology, and rehabilitation: "Is Clinical VR ready for Primetime?". While many well-thought-out VR-based research prototypes have generated a provocative scientific literature and a fair share of excitement, how far are we away from mainstream availability, adoption, and implementation? To address this question, the current article will briefly describe VR technology, discuss the trajectory of Clinical VR over the last 20 years, and summarize the assets that VR offers for creating clinical applications. The discussion section addresses the question of readiness based on an assessment of the theoretical basis for VR relevant to clinical applications, the science to date in specific areas of use, the pragmatic factors regarding availability, usability, and costs of Clinical VR content/systems, and the ethical issues for the safe use of VR with clinical populations. Some of the discussion in the current paper includes topics that have been discussed in previous papers, which may be consulted for additional reading (Lange, Koenig, Chang, McConnell, Suma, Bolas, & Rizzo, 2012; Rizzo, Buckwalter, & Neumann, 1997; Rizzo, Schultheis, Kerns, & Mateer, 2004).

What is Virtual Reality?

The concept and definition of Virtual Reality has been subject to debate by scientists and clinicians over the years. VR has been very generally defined as a way for humans to visualize, manipulate, and interact with computers and extremely complex data (Aukstakalnis & Blatner, 1992). From this baseline perspective, VR can be seen as an advanced form of human-computer interaction (Rizzo et al., 1997) that allows a user to more naturally interact with computers beyond what is typically afforded with standard mouse and keyboard interface devices. Moreover, some VR formats enable users to become immersed within synthetic computer-generated virtual environments. However, VR is not defined or limited by any one technological approach or hardware set up. The creation of an engaged VR *user experience* can be accomplished using combinations of a wide variety of interaction devices, sensory display systems, and content presented in the virtual environment. Thus, there are three common variations for how VR can be created and used.

Non-immersive VR is the most basic format and is similar to the experience of someone playing a modern computer or console videogame. Content is delivered on a standard flat-screen computer monitor or TV with no occlusion of the outside world. Users interact with three-dimensional (3D) computer graphics using a gamepad, a joystick, specialized interface devices (from a treadmill to a handheld *Nintendo Wii remote*), as well as basic mouse or keyboard. Modern computer games that support user interaction and navigation within such 3D worlds, even though presented on a flat-screen display, can technically be referred to as VR environments.

Immersive VR can be produced by the integration of computers, head-mounted displays (HMDs), body-tracking sensors, specialized interface devices, and 3D graphics.

These set-ups allow users to operate in a computer-generated simulated world that changes in a natural or intuitive way with head and body motion. Using an HMD that occludes the user's view of the outside world, an engaged immersive virtual experience employs head and body-tracking technology that senses the user's position and movement and sends that information to a computing system that can update the sensory stimuli presented to the user in near real-time, contingent on user activity. This serves to create the illusion of being immersed "in" a virtual space, within which users can interact. When immersed within computer-generated visual imagery and sounds of a simulated virtual scene, user interaction produces an experience that corresponds to what the individual would see and hear if the scene were real. Another less common method for producing immersive VR experiences uses stereoscopic projection screens arrayed around a user in various configurations. Sometimes six-walled projection rooms known as cave automatic virtual environments (CAVEs) (Cruz-Neira et al., 1993; DeFanti et al., 2011) are used that allow for interaction in a less encumbered, wide field of view simulated environment for multiple concurrent users. However, such CAVE systems are more costly and complex, and are typically beyond the practical resources of most clinical service providers and/or basic researchers.

Regardless of the technical approach, the key aim of these immersive systems is to perceptually replace the outside world with the virtual world to psychologically engage users with simulated digital content designed to create a specific user experience. Immersive VR (most commonly delivered in an HMD) is typically the choice for applications where a controlled stimulus environment is desirable for constraining a user's perceptual experience within a specific synthetic world. This format has been often used in Clinical VR applications for anxiety disorder exposure therapy, analgesic distraction for patients undergoing acutely painful medical procedures, and in the cognitive assessment of users to measure performance under a range of systematically delivered challenges and distractions.

A Very Brief History of Clinical Virtual Reality

VR has recently captured the public's imagination as the next big thing in media. However, the technology for creating VR experiences and its clinical use has existed for at least two decades. During the 1990s the growing availability and rapid evolution of personal computing drove the global adoption of innovative digital technologies for the purposes of productivity enhancement, communication, and social interaction. At the same time, the advances in modern computing power required to automate processes and store/analyze vast quantities of data did not go unnoticed by clinical researchers and providers, who imagined and prototyped novel behavioral healthcare applications. Primordial efforts from this period can be seen in developments that aimed to use personal computers to enhance productivity in patient documentation and record-keeping, automate the administration and scoring of psychometric tests, and in the computer-delivery of cognitive training/rehabilitation activities (Robertson, 1990). As well, with the rapid improvements in internet connectivity seen during the 1990s, the idea of enhancing access to care via internet-based teletherapy (Cuijpers, van Straten, & Andersson, 2008; Putrino, 2014; Rizzo, Strickland, and Bouchard, 2004; Stamm, 1998) and self-help cognitive behavioral programs (Carlbring et al., 2001 Spek et al., 2007) was explored. Since that time, the impact of computer and information technology on society has grown dramatically. This can be seen in the current adoption and growing demand for mobile devices, high speed network access, smart televisions, social media sites, photorealistic digital games, wearable behavioral sensing devices, and now, the 2^{nd} coming of Virtual Reality. Such consumer-driven technologies, thought of as visionary just 10 years ago, have now become increasingly common and essential fixtures in the digital landscape of a global society.

The idea of using VR for clinical purposes was first recognized in the early-to-mid 90s with initial efforts to design VR simulations to deliver exposure therapy for specific phobias (e.g., fear of heights, flying, spiders, and public speaking) (Lamson, 1994; Rothbaum et al., 1995) and for cognitive rehabilitation (Brown et al., 1998; Cromby et al., 1996; Pugnetti et al. 1995; Rizzo, 1994). The compelling feature that drove this innovation was that VR could leverage computing beyond its cardinal purpose - the automation of processes - to instead use computers to produce and deliver sensory stimuli for the creation of embodied. interactive, and immersive user experiences. This was recognized early on in the visionary article "The Experience Society" by VR pioneer, Myron Krueger (1993), in his prophetic statement that, "... Virtual Reality arrives at a moment when computer technology in general is moving from automating the paradigms of the past, to creating new ones for the future." (p. 163). Viewed from this perspective, VR afforded the opportunity to create highly realistic, interactive, and systematically controllable stimulus environments that users could be immersed in, and interact with, for human performance measurement and training, as well as clinical assessment and intervention. Clinicians and scientists who were drawn to the idea of VR during this time were often guided by the belief that its core features and assets could support the development of innovative clinical approaches that were not possible with existing traditional methodologies.

The added value for such VR systems can be seen in the technology's capacity to create systematic human testing, training, teaching, and treatment environments that allow for the precise control of complex, multi-sensory, dynamic 3D stimulus presentations. Within such simulations, sophisticated behavioral interaction is possible and such physical activity can be precisely tracked, recorded, and analyzed to study human performance and behavior. Much like an aircraft simulator serves to test and train piloting ability under a wide variety of controlled conditions, VR can be used to create relevant simulated environments where the assessment and treatment of cognitive, emotional, and sensorimotor processes can take place under stimulus conditions that are not easily deliverable and controllable in the physical world. When combining VR's stimulus control features with the ability to immerse users in functional and ecologically relevant virtual environments, early Clinical VR scientists envisioned a fundamental advancement in how human assessment and intervention could be addressed. It could be conjectured that this "Ultimate Skinner Box" perspective was what human experimental researchers and clinicians had always strived for. but were limited by the constraints imposed by the laws of physics that govern physical reality. This "vision" drove the enthusiasm and innovative efforts seen in the fledgling area of Clinical VR in the 1990s.

Unfortunately, many technical challenges needed to be overcome before this vision of Clinical VR could be achieved. When discussion of the potential use of VR for human research and clinical intervention first emerged in the 90s, the technology needed to deliver on this vision was not sufficiently mature. Consequently, during these early years VR suffered from a somewhat imbalanced "expectation-to-delivery" ratio, as most who explored VR systems during that time will attest. Computers were too slow, 3D graphics were primitive, and user interface devices were awkward, requiring more effort than users were willing to expend to learn how to operate them effectively. Moreover, VR HMDs were costly, bulky, and had limited tracking speed, resolution, and field of view. As a consequence, VR commenced its "nuclear winter" period in 1995 as the public became disenchanted with the quality of a typical VR experience and generally viewed it as a failed technology. Thus, VR languished for many years in what the Gartner Group has termed "the trough of disillusionment", the stage in technology adoption that often follows the "peak of inflated expectations" period described in their regularly updated "Hype Cycle for Emerging Technologies" (Gartner, 2016).

In spite of these technical challenges, the core vision of Clinical VR was sound and VR "enthusiasts" continued to pursue the research and development needed to advance the

technology and document its added clinical value. And, over the last 22 years, the technology for creating VR systems gradually caught up with the vision of creating compelling, usable, and effective Clinical VR applications. This has been possible in large part due to the gradual, but continuous, advances in the underlying VR-enabling technologies and methods (e.g., computational speed, computer graphics, panoramic video, audio/visual/haptic displays, natural user interfaces, tracking sensors, speech and language processing, artificial intelligence, virtual human agents, authoring software, etc.). Such advances have resulted in the technical capability needed to support the creation of lowcost, yet sophisticated, immersive, and interactive VR systems, capable of running on commodity-level computing devices. In part driven by the digital gaming and entertainment sectors, and a near insatiable global demand for mobile and interactive networked consumer products, these advances in technological "prowess" and accessibility have provided the hardware and software platforms needed to produce more adaptable and high-fidelity Clinical VR scenarios. This has created a state of affairs where Clinical VR applications can now usefully leverage the interactive and immersive assets that VR affords as the technology continues to get faster, better, and cheaper moving forward toward the third decade of the 21st Century! Moreover, since the 1990s a significant scientific literature has evolved, almost under the radar, reporting many positive outcomes across a range of clinical applications that have leveraged the assets provided by VR (Botella et al., 2015: Dascal et al., 2017; Freeman et al., 2017; Hoffman et al., 2011; Howard, 2017; Maples-Keller et al., 2017; Morina et al., 2015; Rizzo et al., 2015ab; Rose et al., 2005; Slater & Sanchez-Vives, 2016).

A short list of the areas where Clinical VR has been usefully applied includes fear reduction in persons with specific phobias (Morina et al., 2015; Opris et al., 2012; Parsons and Rizzo, 2008a; Powers and Emmelkamp, 2008), treatment for posttraumatic stress disorder (PTSD), depression, and paranoid delusions (Beidel et al., 2017; Botella et al., 2015; Difede et al., 2007, 2013; Falconer, et al., 2016; Freeman et al., 2016; Rizzo et al., 2010, 2013, 2015a; Rothbaum et al., 2001, 2014), discomfort reduction in cancer patients undergoing chemotherapy (Chirico et al., 2016; Schneider et al., 2010), acute pain reduction during wound care and physical therapy with burn patients (Hoffman et al., 2011) and in other painful procedures (Gold et al., 2006; Mosadeghi et al., 2016; Tashjian, et al., 2017; Trost et al., 2015), body image disturbances in patients with eating disorders (Riva, 2011), navigation and spatial training in children and adults with motor impairments (John et al., 2017; Rizzo et al., 2004; Stanton et al., 1998), functional skill training and motor rehabilitation in patients with central nervous system dysfunction (e.g., stroke, traumatic brain injury (TBI), spinal cord injury (SCI), cerebral palsy, multiple sclerosis, etc.) (Deutsch & McCov, 2017; Holden, 2005; Howard, 2017; Klamroth-Marganska et al., 2014; Lange et al., 2012; Merians et al., 2002, 2010), and for the assessment and rehabilitation of attention, memory, spatial skills, and other cognitive functions in both clinical and unimpaired populations (Bogdanova, Yee, Ho, & Cicerone, 2016; Brooks et al., 1999; Brown et al., 1998; Matheis et al., 2007; Ogourtsova, Silva, Archambault, & Lamontagne; 2015; Parsons, Rizzo, Rogers, and York, 2009; Passig, Tzuriel, & Eshel-Kedmi, 2016; Pugnetti et al., 1995; Rizzo, 1994; Rizzo et al., 2006; Rose et al., 2005; Valladares-Rodriguez et al., 2016). To do this, Clinical VR scientists have constructed virtual airplanes, skyscrapers, spiders, battlefields, social settings, beaches, fantasy worlds, and the mundane (but highly relevant) functional environments of the schoolroom, office, home, street, and supermarket. In essence, VR environments mimicking real or imagined worlds can be applied to engage users in simulations that support the aims and mechanics of a specific clinical assessment or therapeutic approach. As a result, there is a growing consensus that VR has now emerged as a promising tool in many domains of research (Bohil et al., 2011; Larson, Feigon, Gagiardo, & Dvorkin, 2014) and clinical care (Goldman-Sachs, 2016; Freeman et al., 2016; Lange et al., 2012; Norcross et al., 2013).

Analysis of Clinical VR Assets

What makes Clinical VR so distinctively innovative is that it represents more than a simple linear extension of existing computer technology for human use. By way of VRs capacity to immerse a user within an interactive computer-generated simulation, new possibilities exist that can go beyond the simple automation of previous clinical assessment and intervention approaches. Nevertheless, in deciding as to whether Clinical VR is ready for primetime, one needs to consider what features VR offers that may make it especially suited for clinical and research usage.

On a very general level VR can be seen to foster core processes that are relevant across a variety of clinical domains. These processes can be briefly summarized as expose (e.g., exposure therapy for anxiety disorders, PTSD, or addiction treatment), distract (e.g., distracting attention away from painful medical procedures to reduce pain perception or promote discomfort reduction), motivate (e.g., motivating clients in cognitive/physical rehabilitation to perform repetitive and sometimes boring tasks by embedding them within game-like contexts), measure (e.g., measuring performance on physical/cognitive assessment activities), and engage (e.g., generally seen as the captivation of attention/action that is useful for engaging participation with clinical applications). To effectively drive these processes in a thoughtful fashion, it is helpful to be aware of the features and assets that are available for clinical use of VR technology. These assets have been specifically detailed as they relate to the predecessor field of aviation simulation technology (Jentsch & Curtis, 2017) and an earlier detailing of these assets for neuropsychology appeared in Rizzo et al. (2004). However, in view of the rapidly advancing state of VR technology, a revisiting of its current status is warranted, especially as it pertains to general clinical applications.

Ecological Relevance

Clinical VR scenarios can be modeled after relevant contexts that exist in everyday life. Within such simulated environments, it is possible to create activities that mimic challenges faced by clinical populations, and implement them as part of assessment and intervention strategies. This has been a guiding feature in Clinical VR development since the 1990s, leading to the creation of many standard archetypic testing and treatment spaces (e.g., homes, offices, classrooms, stores, tall buildings, cars, battlefields, hospital settings, social gatherings, public speaking auditoriums, etc.). The primary driver for these efforts is the view that we can better predict or enhance human functioning (e.g., behavioral outcomes, emotional coping, cognitive/motor task performance) in the real world by providing systematic and highly controllable assessments and interventions *within* functionally similar virtual worlds.

This is particularly relevant in view of the underlying concepts of generalization and transfer of training that have been "big" issues across all domains of psychology and rehabilitation. For example, traditional neuropsychological assessment and rehabilitation has been criticized by some authors (Parsons, Carlew, Magtoto, & Stonecipher, 2015; Rizzo, Buckwalter, & Neumann, 1997; Sbordone, & Long, 1996; Wilson, 1997) as limited in the area of ecological validity, that is, the degree of relevance or similarity that a test or training system has relative to the "real" world (Neisser, 1978). A number of examples illustrate efforts to enhance the ecological validity of assessment and rehabilitation by designing VR scenarios that are "replicas" of relevant archetypic functional environments. This has included the creation of virtual cities (Brown et al., 1998; Costas, Carvalho & de Aragon, 2000; Gamito et al., 2016), supermarkets (Cromby et al., 1996; Josman et al., 2014; Levy et al., 2015); homes (Koenig, 2012; Rose et al., 2001); kitchens (Christiansen et al., 1998; Davies et al., 1998; Foloppe et al., 2015; Wall et al., 2017), school environments (Rizzo et

al., 2000, 2006; Stanton et al., 1998), workspaces/offices (Koenig et al., 2012; Krch et al., 2013; Matheis et al., 2007; McGeorge et al., 2001); rehabilitation wards (Brooks et al., 1999) and even a virtual beach (Elkind et al., 2001). From these efforts, recent reviews have provided support for the impact of ecologically-relevant Clinical VR applications on real world treatment outcomes in both clinical psychology (Morina et al., 2015) and in rehabilitation (Howard, 2017).

While early attempts at the creation of these environments varied significantly in their level of pictorial or graphical realism, this fidelity factor may be secondary in importance. relative to the actual activities that are carried out in the environment for determining their value from an ecological relevance standpoint (cf. Parsons, 2015; Rizzo et al., 2006). Interestingly, when in a virtual environment, humans often times display a high capacity to "suspend disbelief" and respond as if the scenario was real. It could be conjectured that the "ecological value" of a VR task that needs to be performed may be well supported in spite of limited graphical realism. In essence, as long as the VR scenario "resembles" the real world, possesses design elements that replicate key real-life challenges, and the system responds well to user interaction, then the graphical realism can be less important for activating behavior and emotion. This has especially been observed by clinicians using VR to conduct exposure-based therapies for anxiety disorders. PTSD, and addiction (Bordnick et al., 2013). Clients commonly report significant emotional activation in spite of the "cartoonish" nature of the visual content seen in some VR scenarios. Thus, while a number of the successful VR scenarios designed for exposure-based therapy of specific phobias would never be mistaken for the real world, clients experiencing these VR worlds still manifest physiological responses and report subjective units of discomfort levels that suggest they are responding "as if" they are in the presence of the feared stimuli (Costanzo et al., 2014; Norrholm et al., 2016; Wiederhold & Wiederhold, 1998).

The recent advances in computer graphics as seen in modern computer games have now made the "fidelity" issue less of a concern. As well, the growing popularity of panoramic 360-degree cameras and photogrammetry has provided an affordable means to create photorealistic content for VR applications. While expectations of computer graphics have also increased steadily, especially with a younger generation that has grown up with computer and console games and may be put off by low-quality graphics, perceptually convincing VR scenarios are now more the norm than the exception in current VR development. Although it is yet to be documented that increased realism has had an impact on improving clinical outcomes, the ability to create more compelling visual VR content may, at the very least, improve face validity and increase user buy-in from patients and clinical end-users.

Systematic delivery and control of sensory stimuli

One of the cardinal assets of any advanced form of simulation technology involves the capacity for systematic delivery and control of stimuli. This asset provides significant opportunities for developing Clinical VR methods. In fact, one could conjecture that the systematic delivery and control of stimuli in a testing or treatment environment provides the basic foundation of all human research and clinical methodologies along with the subsequent capture and analysis of the behavior that occurs in response to those conditions. In this regard, an ideal match exists between the stimulus delivery assets of VR simulation systems and the requirements of any clinical assessment and intervention procedure. This can be seen as a core asset whether one is testing construct-specific cognitive processes (e.g., selective attention performance contingent on varying levels of stimulus intensity and distraction) (Rizzo et al., 2006; Mühlberger, 2016), to the complex targeting of more molar functional behaviors (e.g., planning and initiating the steps to function within a complex office or home setting) (Keefe et al., 2016; Krch et al., 2013), to the precise titration of anxiety

activating content in the service of pacing exposure therapy for the treatment of phobias or PTSD (Rizzo et al. 2015a; Rothbaum et al., 1995,1999).

Moreover, the precise control over multiple concurrent tasks and presentation of realistic distractions during these tasks presents a unique opportunity to simulate complex, lifelike scenarios that is only starting to receive attention in Clinical VR research and development. This approach stands in stark contrast to the traditional single-construct exposure to cognitive tasks in distraction-free environments such as a clinician's office.

This capacity for systematic stimulus control within the context of ecologically relevant simulations of everyday life (i.e., The Ultimate Skinner Box) for assessment and intervention purposes is one of the key areas that differentiate Clinical VR from all previous methodologies. Thus, VR's stimulus delivery capability has been recognized as a significant asset for supporting the integration of VR with brain imaging and psychophysiology studies (Bohil et al., 2011; Chou et al., 2012; Costanzo et al., 2014; Norrholm et al., 2016; Tarr & Warren, 2002). This is especially relevant for the field of neuropsychology which has been increasingly integrating advanced neural imaging technologies (e.g., fMRI, DTI, SPECT, QUEEG, CT, etc.) in its quest for a better accounting of the structure and processes underlying brain/behavior relationships. In fact, the use of VR in imaging studies has nearly as long a history as the direct use of the technology for clinical interventions (Astur et al., 1998).

For example, a VR simulation of the Morris Water Maze test of spatial navigation and place learning, commonly used with rodents, has generated significant research examining the role of the hippocampus in human learning (Astur et al., 1998, 2002, 2004). In this elegant and well-matched use of VR, a human user must navigate a space to find a hidden platform using visual cues in the surrounding environment. Used in conjunction with fMRI, the test has been applied to assess place learning performance while concurrently measuring hippocampal activity. Research with this VR system has reported poorer performance and decreased activation in health conditions where the hippocampus is implicated such as with Alzheimer's disease (Shipman & Astur, 2008), PTSD (Astur et al., 2006), and schizophrenia (Folley et al., 2010). Other researchers have similarly integrated VR and brain imaging and have reported, reduced activation of pain-related regions of interest using VR as a distractor from experimentally induced pain (Hoffman et al., 2006, 2011); changes in brain activation (i.e., amygdala and 3 frontal areas) to VR stimuli following exposure therapy for PTSD (Roy et al., 2010, 2014); neural predictors of change in emotion recognition in persons on the autism spectrum using VR social cognition training (Yang et al., 2017); and cortical reorganization and associated locomotor recovery in chronic stroke patients with VR game-based rehabilitation (You et al., 2005). In a recent effort to combine a virtual classroom scenario with Near-Infrared Spectroscopy (NIRS), Blume et al., (2017) in collaboration with Katana Simulations, created an immersive virtual classroom neurofeedback training to treat deficits associated with attention-deficit hyperactivity disorder (ADHD; Blume et al., 2017). A clinical trial is currently evaluating the efficacy of the training, that utilizes the NIRS signal to control the classroom's lighting intensity as a feedback mechanism. It is hypothesized that a training protocol of 15 sessions, containing activation and deactivation trials, will facilitate self-regulation skills, and improve ADHD symptoms and motor activity in the participating 90 children with ADHD. Participants are randomly assigned to the NIRS-based training in the VR classroom, a NIRS-based training in a 2D classroom, or an electromyogram-based training in VR. This clinical trial is ongoing.

Although head movement is restricted in most brain imaging systems (excluding NIRS), specialized "magnet-friendly" interaction devices and displays, can still allow users to engage with dynamic virtual content, albeit the experience is different than a typical unrestricted VR application. With that limitation acknowledged, the integration of VR as a tool for delivering complex, interactive stimuli with advanced brain imaging techniques may

support neuropsychology in reaching its stated purpose, that of determining unequivocal brain-behavior relationships, in addition to advancing the state of the science in other clinical disciplines.

Delivery of strategic real-time performance feedback

VR simulations can be designed to provide users with feedback as to the state of their performance during task practice (knowledge of performance) and after task completion (knowledge of results) (Levin, Weiss, & Keshner, 2015). A primary aim is to promote behavioral calibration of the clients' actions using clear signals that indicate their status towards achieving performance outcomes. However, careful consideration needs to be placed on the use of positive and negative feedback during and after correct and incorrect performance to balance short-term and long-term goals as they relate to user motivation and task performance (Burgers et al., 2015). Delivery of feedback stimuli can appear in graded (degree) or absolute (correct/incorrect) forms and can be presented via auditory, visual, or tactile sensory modalities depending on the goals of the application and the needs of the user. Moreover, feedback can be inherent to the task and the way the user's actions are represented in the VR environment. For example, representing the user's hands through virtual models is also a form of feedback, providing real-time information about the user's movements. This feedback can be modulated, such as exaggerating, dampening, slowing down, speeding up, or even mirroring movement (e.g. Regenbrecht et al., 2014), depending on the user's therapeutic goals.

Feedback delivery is an intuitively essential component for rehabilitation efforts as it is generally accepted to be necessary for most forms of learning or skill acquisition (Levin, Weiss, & Keshner, 2015; Sohlberg & Mateer, 1989; 2001). While VR-based feedback can be presented to signal performance status in a form that wouldn't naturally occur in the real world (e.g., a soft tone indicating a correct response), more relevant or naturalistic sounds can also be creatively applied to enhance both ecological relevance and the believability of the scenario. For example, in a VR application designed to help children with learning disabilities practice escape from a house fire (Strickland, 2001), the sound of a smoke detector alarm raises in volume as the child gets near to the fire's location. As the child successfully navigates to safety, the alarm fades contingent on her choosing the correct escape route. More recently, Jin et al. (2016) have implemented a biofeedback methodology for users aiming to reduce chronic pain via treadmill interaction within a virtual forest walking task. As users lower their level of skin conductance level (as part of an effort to teach relaxation and mindfulness strategies), the "fog" within the forest gradually lifts to reveal an engaging and idyllic wilderness setting. Physical rehabilitation applications have also leveraged the strategic delivery of performance feedback to enhance relearning of upper extremity abilities following stroke or traumatic brain injury (Adamovich et al., 2009; Badia et al., 2016; Deutsch, Latonio, Burdea, & Boian, 2001; Jack et al., 2001; Klamroth-Marganska, et al., 2014).

Delivery of cueing stimuli to guide successful performance and impact behavior

The capacity for dynamic stimulus delivery and control within a virtual environment also supports the presentation of cueing stimuli that can be used to guide user performance. This is especially relevant for cognitive rehabilitation applications that implement "error-free" learning strategies. Error-free training in contrast to trial and error learning has been shown to be successful in a number of non-VR investigations with diverse test populations including persons with developmental disabilities, schizophrenia, and CNS disorders (Fish et al., 2015; Wilson et al., 1994, 1996). This asset underscores the idea that for some clinical approaches it may *not* be desirable for VR to simply mimic reality with all its opportunities for error. Instead, cueing stimuli features that are not easily deliverable in the real world can be

presented in the virtual world to help guide and train successful performance. In this special case of stimulus delivery, cues are given to the user *prior* to a response in order to help guide successful error-free performance.

While the use of cueing to support errorless learning is compelling and can now be easily programmed as a feature within VR simulations, it has rarely been applied and tested in VR contexts. In the only VR-based head-to-head comparison of this type, Connor et al. (2002), reported on a series of case studies of users with TBI operating a haptic joystickmediated "Trails B" type training task. In the error-free condition, the haptic joystick restricted movement on the non-immersive Trails task such that the user was not allowed to make navigation errors. Mixed findings were reported, but error-free training resulted in significant response speed improvements compared to trial and error training in some cases. In a case report. Brooks et al. (1999) used error-free training for wayfinding in a rehabilitation ward as one component in a VR training system that produced positive transfer to the real ward. Harrison et al. (2002) also reported the use of cueing stimuli in a VR system designed to train maneuverability and route-finding in novice motorized wheelchair users. Arrows were presented to trainees with the caption "Go this way" to guide successful route navigation whenever the user would stray into areas where invisible "collision boxes" were programmed in the environment. Two patients with severe memory impairments took part in route finding training over the course of seven days with the patients successfully learning two subsections of the test routes while failing to eradicate errors on two further subsections of the routes. Cueing was also incorporated into a VR system designed for executive function assessment and training in the context of a series of food preparation tasks within a virtual kitchen scenario (Christiansen et al., 1998). This VR scenario assessed the ability to perform 30 discrete steps required to prepare a can of soup and make a sandwich using both visual and auditory cues to prompt successful performance. However, the specific effect of this cueing was not isolated, nor was a system in place to prevent errors from actually occurring. Finally, a more recent case report has shown positive gains in a user with Alzheimer's disease using a similar virtual kitchen (Foloppe et al., 2015). Generally, it appears that the use of cueing stimuli to support error-free VR rehabilitation is promising in concept but there is currently only limited research support with its use in VR. However, while empirical support is still lacking, the ease for programming these components within VR make it an appealing feature to test more rigorously in future research.

Beyond errorless learning for cognitive rehabilitation, perhaps the use of verbal cueing could be applied for cognitive behavioral approaches that address self-talk within provocative VR settings. For example, if key prompting statements could be specified in advance, users could pre-record supportive self-talk cues in their own voice. These cues could then be played back to the user in a modulated "dreamlike" vocal tone during strategic points within a socially stressful VR scenario designed to help users deal with anger management, social phobia, or shyness issues. This form of natural "inner-voice" guidance might be useful for self-talk methods within virtual social scenarios with the aim to improve generalization of the user's self-generated sub vocal cognitions that could facilitate more optimal social interaction in the real world.

A dramatic extension of this type of proposed self-cueing feature worth mentioning involves recent innovative VR efforts to address the cognitive distortions of persons with depression (Falconer et al., 2016). With the goal of improving "self-compassion", clinically depressed users were invited to enter a virtual world for 8 minutes where they were requested to "console" a distressed virtual child using tactics on which they had received prior coaching. After a short period of time, the user was switched into the role (and virtual body) of the child and presented with a replay of *their own attempts* at consoling the child. The replay was delivered by an adult virtual representation of themselves that expressed their own consoling words back to them in their own voice captured from their previous verbalization and behavioral activity with the virtual child. In a small initial trial (n=15), after

three repetitions of this body-swapping scenario, significant reductions were measured in depression severity and self-criticism, along with a significant increase in self-compassion, from baseline to 4-week follow-up. Four patients showed clinically significant improvement. Although this effect should still be considered preliminary, it does underscore the potential for Clinical VR to present sophisticated cueing content, in this case a fully naturalistic rendition of self-delivered, self-compassion, that produced significant emotional impact on users in a fashion that would be near impossible to deliver with previously existing methods.

Behavioral performance capture and retrospective and intuitive after action reviews

The review of a client's behavioral performance in any assessment and training activity typically involves examination of numeric data and subsequent translation of that information into graphic representations in the form of tables and graphs. Sometimes videotaping of the actual event is used for a more naturalistic review and for behavior rating purposes. These methods, while of value, are typically quite labor intensive to produce, and sometimes result in a less than intuitive method for visualizing and understanding a complex performance record. These challenges are compounded when the goal of the review is to provide feedback and insight to clients whose impairments may preclude a useful understanding of traditional forms of data presentation. VR offers the capability to capture and review a complete digital record of performance in a virtual environment from many perspectives. For example, performance in a virtual environment can be later observed from the perspective of the user, from the view of a third party or position within the scenario, and from what is sometimes termed, a "God's eye view", from above the scene with options to adjust the position and scale of the view. This can allow a client to observe and repeatedly review their performance from multiple perspectives. Options for this review also include the modulation of presentation as in allowing the client to slow down rate of activity and observe each behavioral step in the sequence in "slow motion" (Rizzo et al., 2004).

Advanced programs that incorporate such methods have been in steady use by the military to conduct what is termed After Action Reviews (AAR) (Morrison & Meliza, 1999). In military VR applications that often include multiple participants in a shared virtual space, a computerized AAR tool can allow the behavior of any participant to be reviewed from multiple vantage points at any temporal point in the digital training exercise. This is now standard procedure for military simulation training, but has had limited application in Clinical VR approaches. With the exception of less naturalistic review of paper and pencil results and the occasional review of a client's videotaped performance from fixed camera positions, the capacity to provide more intuitive "first-person" perspective views to clients has not been feasible with existing technology, and thus VR now provides a powerful asset in this area (Rizzo et al., 2004).

Early efforts to leverage this VR asset appeared as a feature for reviewing navigational performance in a number of wayfinding and place learning applications (Astur, Oriz & Sutherland, 1998; Jacobs, Laurance & Thomas, 1997; Kober et al., 2013; Koenig, Crucian, Dalrymple-Alford, & Dünser, 2010; Skelton et al., 2000). This has primarily been used in applications where a tracked movement record is vital for measuring and visualizing the dependent variable of exploratory behavior. A review method was also developed for replaying a child's head movements while they are tracking stimuli within a virtual classroom in a VR assessment of attention (Rizzo et al., 2006). This application took data from a tracking device positioned on top of the VR HMD and represented the captured movement via a virtual representation of a person's head. The virtual head is rendered to face outward from the screen and a "straightforward" head position represents the attentive gaze at the virtual blackboard where target hit stimuli are displayed to the child. During video playback after a test session, it is possible to observe the child's head movements during discrete periods when distracting stimuli are presented around the classroom (see:

https://youtu.be/BQyO3oDMKbl). Head movements away from the center of the screen represent the child's actual movements to follow the distracting stimuli on each side of the classroom instead of the face forward position required to view the target stimuli. This playback format delivers an extremely intuitive understanding of the distractibility of children diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) during VR classroom performance testing that were revealed from the complex statistical analyses of this movement data. The provision of this type of intuitive behavioral visualization could serve to improve the understanding of the behavior of an ADHD child by professionals, parents, and perhaps even the tested child in a manner not possible with graphs and data tables (Rizzo et al., 2004; 2006). Systematic studies of the clinical use of this form of performance record review have yet to appear in the literature, although this form of visualization asset illustrates how VR may add value for assessment and intervention that is not readily available with existing traditional tools.

The "Pause Button" for mid-session review and analysis with the clinician

In any intervention that activates cognitive, behavioral, and emotional processes for a clinical purpose, clinician review/feedback is an essential component for building a therapeutic alliance and fostering clients' self-awareness. While feedback can be delivered digitally within a simulation for guiding real time performance, and retrospectively for past performance review (see previous three assets), Clinical VR interactions can be paused and restarted at precisely the next moment in the digital sequence or replayed from an earlier juncture for the purposes of face-to-face therapist engagement/support as needed. It is easy to think of VR as an all-encompassing computerized environment that delivers all the ingredients for good intervention, but that would be naïve. Rather, the use of such potent and emotionally evocative simulations should be viewed simply as tools for extending the skills of a well-trained clinician and as a method that may amplify client engagement with a therapeutic process that is known to have efficacy in a real-world delivery context. From this view, the capacity to pause a simulation to engage in clinical dialog at strategic junctures is a distinction that is often overlooked due to its simplicity. This functionality has relevance across all areas of clinical intervention and needs to be specifically designed during the VR development process to augment the therapist-client relationship instead of hindering it.

Specifically, immediate therapist response to client performance is one form of feedback that is commonly seen in the rehabilitation of clinical populations. This may be of particular value for clinical populations who have memory difficulties that require more frequent review and feedback during a training session. While pausing is of course possible with any assessment or intervention approach, VRs unique assets offer the opportunity to pause or "freeze time" in the middle of a functional "real world" simulated task. This can result in additive learning benefits, whereby you can "stop and evaluate" not only individual performance, but also by examining what environmental elements may be affecting performance. For example, during activities in a VR kitchen for the completion of a simple task (i.e., making a can of soup), performance may be paused for the correction of errors (missed procedure steps), evaluation of safety elements of the task (where are the sharp objects) or discussion of perceptual difficulties (inappropriate visual scanning) (Rizzo et al., 2004). The simulation can then be restarted or backed up to an earlier point to allow for a "redo". Similarly, for psychological treatment, when a user is immersed within a provocative simulation where they are confronting a digital recreation of a traumatic event or an environment designed to deliver anger or addictive behavior cues, the simulation can be paused for direct coping strategy coaching with the clinician.

Thus, the ability to pause performance "mid-digital stream" allows a clinician to intervene strategically to enhance client processing and discussion of decision-making, memory strategies, coping behaviors, assertive language, cognitive restructuring, or any of

the myriad clinical tactics that are commonly applied as the elements of quality evidencebased (and empathy-based) therapeutic care. Contrary to some of the negative concerns we have heard expressed over the years regarding the use of technology in clinical practice ("it puts a barrier between the therapist and the client"), the ability to pause (and later restart) a client's simulated experience for a direct clinical intervention may actually serve to *remove* a key barrier—the lack of an immediate shared experience. Therapy can involve a lot of discussion of abstract concepts that sometimes don't lend themselves to an easily shared understanding of the client's experience of everyday life. A clinician who has the opportunity for close observation of the client's behavior within an emotionally or cognitively challenging VR simulation, and who then can pause it to provide strategic support or reflection, may have an edge for developing a closer understanding of the client. This edge may reside in the clinician's newfound ability to observe the client as they address a challenge that would have previously remained unseen by the clinician due to its exclusive occurrence outside of the therapy office.

Safe testing and training environments that minimize the risks due to errors.

This is an area where Clinical VR provides an obvious asset by creating options for users with cognitive or sensorimotor impairments to be tested and trained in the safety of a simulated digital environment. The value of this has already been amply demonstrated in the predecessor field of aviation simulator research where actual flying accidents dropped precipitously following the early introduction of even very crude aircraft simulation training (Johnston, 1995). Early on in the Clinical VR domain, this asset served as a driving force for VR system design and research with both clinical and unimpaired populations. For example, the simple (but potentially dangerous) act of street crossing has been tested and trained in VR with unimpaired children (McComas, MacKay, & Pivak, 2002; Morrongiello, Corbett, Switzer, & Hall, 2015; Schwebel, McClure, & Severson, 2014), populations with learning and developmental disabilities (Brown et al., 1998; Josman, Ben-Chaim, Friedrich, & Weiss, 2008; Strickland, 2001), and adult TBI and stroke groups with neglect (Navarro et al., 2013; Naveh, Katz, & Weiss, 2000). Other relevant application areas include kitchen safety (Rose, Brooks, & Attree, 2000), escape from a burning house with children on the autism spectrum (Strickland, 2001); preventing falls with at risk elderly (Jaffe, 2004; Neri et al., 2017), use of public transportation (Mowafty et al., 1995), and driving with a range of clinical populations (Akinwuntan, Wachtel, & Rosen, 2012; Liu, Miyazaki & Watson, 1999; Pietrzak, Pullman, & McGuire, 2014; Rizzo, Reinach, McGehee, & Dawson, 1997; Schultheis & Mourant, 2001). And, more recently, there has been an increased interest in VR driving applications to reduce risk in both novice and aged populations (Casutt, Martin, Keller, & Jäncke, 2014; Cox et al., 2015). In addition to the goal of promoting safe performance in the real world, some researchers have reported positive results for building a more rational client self-awareness of deficits using a VR approach. For example, Davis and Wachtel, (2000), have reported a number of instances where older adults, post-stroke, had decided not to continue making a return to driving a primary immediate goal after they had spent time in a challenging VR driving system.

Finally, one concern that may exist with this asset involves the potential that practice of activities that are dangerous in real life, within the safety of a VE, might create a false sense of security or omnipotence that would put the client at risk upon subsequent action in the real world. In essence, can *safe* transfer of training occur in the real world when the consequences of errors are prevented from occurring in VR? This is a very challenging concern that needs careful consideration. Perhaps, one option would be to provide a noxious sound cue, contingent on the occurrence of dangerous errors in VR, as a means to condition a proper attitude of caution in clients. This concern further underscores the need for a professional to closely monitor client activity in order to recognize possible patterns of risk taking behavior that could emerge when using VR (Rizzo et al., 2004).

Independent practice of therapeutic activities outside of the clinic

Independent home-based physical therapy or cognitive training by clients following a stroke or TBI is a common and highly recommended component for most approaches to rehabilitation. Similarly, with standard cognitive behavioral therapy (CBT) for psychological disorders, it is generally accepted that by having clients do between-session "homework", that generalization of skills learned in therapy session will be promoted in everyday life. Thus, clients are routinely encouraged to engage in clinician-recommended therapeutic activities independently as part of a general approach to clinical care. Up until the last few years, access to VR technology for supporting clinical care outside of the clinic was a hopeful vision, but very limited by the immature state of the technology. Consequently, there is very little research on the additive value of home-based VR for bolstering clinic-based interventions on clinical outcomes.

Researchers over the last 20 years have proposed and tested various configurations for pushing VR game-based physical rehabilitation into home-based systems (Piron et al., 2001; Proffitt & Lange, 2015; Standen et al., 2014). However, as compelling as this idea sounds in concept, limitations due to the cost of equipment and complexity of set up and use limited the general adoption of this approach. One challenge for physical rehabilitation early on was seen in the need for specialized interface devices and body tracking systems required to foster interaction with virtual rehabilitation task content. This has been somewhat minimized in recent years with various commercially available camera-based 3D tracking systems like the Microsoft Kinect or the Leap Motion sensor. There are a number of commercial and non-commercial entities that develop such VR systems based on low-cost sensors, but they have been primarily focused on clinic-based use (Faria, Andrade, Soares, & Bermudez i Badia, 2016; MindMaze, 2017; SilverFit, 2017). Movement of these systems into the homes of users for independent practice and online tracking of use/performance by a supervising clinician is only starting to become technically feasible and future effort in this area is expected to accelerate, especially in view of the positive findings that have emerged from studies of in-clinic use (Howard, 2017; Klamroth-Marganska et al., 2014).

Efforts to use immersive VR for CBT home-based activities have been similarly hampered by cost and complexity issues. That is also expected to change in the near future as low-cost VR HMDs that are easy to operate are now coming into the marketplace. This is in part due to the widespread access to personal computing, previously limited to standalone computers, but now bolstered by the ubiquitous presence of mobile phones/devices. Thus, access to computing power is no longer a significant bottleneck for supporting independent Clinical VR practice. Moreover, access to a VR HMD for personal use is no longer a limiting factor as new technology has accelerated the availability and adoption of low-cost consumer level HMDs. This can be seen in the rapid developments in mobile phone enabled HMDs. Such products as the Samsung Gear VR or the Google Daydream, offer fairly good fidelity at the price of a mobile phone and a HMD housing costing less than \$100, into which the phone can be inserted to create a working VR headset. These systems are easy to use and there is content that is becoming readily available that can be applied for clinical purposes. For example, low-cost "fear of public speaking" VR software is readily downloadable (Hypergrid Business, 2016) for these systems. The software allows users to practice their speaking skills in front of a wide range of virtual audiences along with the presentation of public speaking coaching content. However, while self-treatment for this form of anxiety when viewed as a skill training intervention appears on the surface to be relatively benign, it does open the door to other types of self-help VR anxiety disorder applications. This state of affairs will require a deeper analysis as to the ethical use of such emotionally evocative software and the issues surrounding VR self-help will be discussed later in this article.

Adaptable user interfaces and sensory displays to promote access

The emerging human computer interaction research area referred to as "3D User Interaction" (LaViola et al., 2017) recognizes that interaction with VR content requires thoughtful attention to both design principles and the needs of the targeted user groups. This is especially relevant for clinical users with sensory or motor impairments where their capacity to receive value from a VR assessment or rehabilitation approach is always governed by their ability to interact with the VR content (Rizzo et al., 2004). While an extensive literature exists in the area of interface design for persons with disabilities (Barrett, McCrindle, Cook & Booy, 2002; Darejeh & Singh, 2013; Lanyi et al., 2012), a full discussion of that area is beyond the scope of this article. However, since VR content can be interacted with using a wide variety of adaptive interface devices, we will briefly address how that capability can be leveraged as an asset for Clinical VR. This is particularly relevant as sensory and motor impairments are commonly seen in persons with central nervous system (CNS) dysfunction. A question that often arises in assessment and rehabilitation, concerns the degree to which a client's performance reflects CNS-based cognitive dysfunction vs. artifacts due to sensorimotor impairments. VR offers two ways in which this challenge may be addressed in the testing and training of cognitive and everyday functional abilities in persons with sensorimotor impairments.

One approach places emphasis on the use of adapted human computer interface devices for VR interaction. Such devices can allow a user with significant motor impairments to interact with VR assessment and training content, beyond what is possible for similar clinical activities in the physical world. Interface adaptations can support interaction by leveraging alternative or augmented movement, speech, expired air, tracked eye movement, and by way of recent advances in brain computer interfaces (Kaplan et al., 2013; Millan et al., 2010; Remsik et al., 2016). One very basic example involves the use of a gaming joystick to navigate in a VR scenario modeled after an amnestic client's rehabilitation unit that was found to be effective for teaching wayfinding around the real unit (Brooks et al., 1999). The authors partially attributed the observed positive training effects to the client's capability for quicker traversing of the VR training world using a joystick compared to what her ambulatory impairments (using a walker) would allow in the real environment. This strategy supported efficient use of training time by increasing the number of training trials that were possible (i.e., 10 trials in VR in the time it would take to complete one with the walker). Quite simply, by minimizing the impact of the user's ambulatory impairments, CNS wayfinding functions could be more efficiently trained.

A second approach can be seen in efforts to tailor the sensory modality of the stimuli presented in the VR world around the needs of persons with visual impairments. The few efforts in this area have mainly attempted to build simulated structures around the use of enhanced immersive 3D audio (Lumbreras & Sanchez, 2000) and tactile stimuli (Connor, 2002). For example, Lumbreras et al. (2000), aiming to design computer games for blind children, created a 3D audio VR system referred to as "AudioDOOM". In this application, blind children used a specialized joystick to navigate the mazelike game environment exclusively on the basis of 3D audio cues (e.g., footstep sounds, doors that "creak" open, echoes, etc.) while chasing "monsters" around the environment. Following varied periods of time in the VE, the children are then given "Legos" to construct their impression of the structure of the layout. The resulting Lego constructions were noteworthy in their striking resemblance to the actual structure of the audio-based layout of the maze. Children using this system (who never actually have "seen" the physical visual world) were able to use the 3D sound cues to create a spatial-cognitive map of the space and then accurately represent this space with physical objects (i.e., Legos, Clay, Sand). Examples of some of these constructions are available on the Internet

(http://www.dcc.uchile.cl/~mlumbrer/audiodoom/audiodoom.html). Such adaptive interaction

approaches in VR offer the potential for factoring out sensorimotor impairments that can confound clear assessment or rehabilitation of functioning in a way that might not be feasible or valid within the constraints of the physical world.

Virtual humans for addressing social interaction and training.

The feasibility for creating Clinical VR applications has advanced in part due to substantial progress in 3D computer graphics rendering that now support the creation of ever more believable context-relevant "structural" VR environments (e.g. combat scenes, homes, classrooms, offices, markets) for clinical purposes. However, the next stage in the evolution of Clinical VR will involve populating these environments with Virtual Human (VH) representations that can engage real human users in credible and useful interactions. This capability has been around since the 1990s, but the previous limitations in graphical rendering, natural language processing, speech recognition, and face and gesture animation made the creation of credible VHs for interaction a costly and labor-intensive process. Thus, until recently VHs existed primarily in the domain of high-end special effect studios that catered to the film or game industry, far from the reach of those who thought to employ them in clinical health applications.

This is not to say that representations of human forms have not previously appeared in Clinical VR scenarios. In fact, since the mid-1990s, VR applications have routinely employed "primitive" VHs (e.g., low fidelity graphics, non-language interactive, limited face and gesture expression) to serve as stimulus elements to enhance the realism of a virtual world simply by their static presence. For example, VR exposure therapy applications for the treatment of specific phobias (e.g., fear of public speaking, social phobia) were successfully deployed using immersive simulations that were inhabited by "still-life" rendered characters or 2D photographic sprites (i.e., static full body green screen captured photo images of a person) (Anderson et al., 2005; Klinger, 2005; Pertaub et al., 2002). By simply adjusting the number and location of such VH representations, the intensity of these anxiety-provoking VR contexts could be systematically modulated with the aim to gradually habituate phobic patients to what they feared, leading to improved functioning in the real world with real people. In spite of the primitive nature of these VHs, phobic clients appeared to be especially primed to react to such representations and thus, they provided the necessary stimulus elements to be effective in these types of exposure-based cognitive behavioral treatment scenarios.

Other clinical applications have also used animated graphic VHs as stimulus entities to support and train social and safety skills in persons with high functioning autism (Padget et al., 2006; Parsons et al., 2012; Rutten et al., 2003) and as distracter stimuli for attention assessments conducted in a virtual classroom (Rizzo et al., 2006). VHs have also been used effectively for the conduct of social psychology experiments, essentially replicating and extending findings from studies conducted with real humans on social influence, conformity, racial bias, and social proxemics (Bailenson & Beall, 2006; Blascovich et al., 2002; McCall et al., 2009).

As the technology has evolved, VH agents can now be created that control computer generated bodies and can interact with users through natural language speech and gesture in virtual environments (Gratch et al., 2002; Rizzo, Kenny, & Parsons, 2011; Rizzo & Talbot, 2016a). Moreover, with advances in artificial intelligence, VHs can engage in rich conversations (Morbini et al., 2014), recognize nonverbal cues (Rizzo et al., 2015b, 2016b; Scherer et al., 2014), improve interactional rapport with users (Park et al., 2013), reason about social and emotional factors (Gratch & Marsella, 2004), and synthesize human communication and nonverbal expressions (Thiebaux et al., 2008). This has resulted in VH agent systems that serve as: virtual patients for training novice clinicians (Rizzo et al., 2011,

2016a; Talbot et al., 2012), job interviewers for training young adults on the autism spectrum to perform better in that context (Bresnahan et al., 2016); clinical interviewers to reduce stigma (resulting in higher endorsement of clinical symptoms) (Rizzo et al., 2015b, 2016b), and as health care guides and clinical support agents (Rizzo et al., 2015b). For example, results from of sample of military service members (SMs) who were interviewed by a VH clinical interviewer before and after a deployment to Afghanistan indicated that SMs revealed more PTSD symptoms to the VH than they reported on the Post Deployment Health Assessment (Rizzo et al., 2016b). In another study using the same VH agent system, civilian users reported less concern about being evaluated, disclosed more personal information, and displayed more sadness in an interview with a VH agent compared to interacting with a VH avatar that they believed was being operated by a human-in-the-loop "Wizard of Oz" controller (Lucas et al., 2014).

Thus, VHs now are capable of fostering interactions with real people that can address a wide variety of clinical concerns. There is a growing literature in this area and it is not hard to see the power of VH applications to foster roleplay training targeting social interaction, anger management, relapse prevention for addiction, and in many other areas where clinical populations could benefit from low social risk interaction with a non-judgmental VH (Albright, 2016; Bickmore et al., 2016; Rizzo et al., 2016b; Tegos et al., 2016; Zhang et al., 2017). Although some authors have expressed legitimate concerns about the role of VH "automation" supplanting the role of clinicians (Innes & Morrison, 2017), VHs applications developed thus far, serve more to fill gaps where a clinical provider is not available, than to aim at replacement of human providers.

Game-Based interaction to enhance motivation and engagement

Plato was reputed to have said, "You can discover more about a person in an hour of play than in a year of conversation." (cited in Moncur & Moncur, 2002). This ancient quote may have particular relevance for future applications of Clinical VR. Observing and/or quantifying a person's approach or strategy when participating in a gaming activity may provide insight into cognitive and psychological functioning similar to the types of challenges found in traditional performance assessments. However, a more compelling clinical direction may involve leveraging gaming features and incentives for the challenging task of enhancing motivation and engagement levels in clients participating in rehabilitation, or any other clinical activity for that matter. For example, one possible factor that may contribute to the mixed outcomes reported in cognitive or physical rehabilitation research may be in part due to the inability to maintain a client's motivation and engagement when confronting them with a repetitive series of retraining challenges, whether using wordlist exercises, range of motion exercises, or real-life functional activities (Rizzo et al., 2004). The benefits of gamification for enhancing psychological interventions have also been detailed in Granic et al. (2014) specifically citing research support of its value for improving cognition (e.g., attention), motivation (e.g., resilience in the face of failure), emotion (e.g., mood management), and social interaction (e.g., prosocial behavior). In this regard, an understanding of gaming features and their integration into VR-based rehabilitation systems to enhance client motivation and subsequent clinical outcomes may be a useful direction to explore.

Rehabilitation, whether cognitive or physical, provides a clear use case for how the integration of gaming features with VR is well-matched to the various requirements for creating effective rehabilitation tasks (Lange et al., 2012; Rizzo et al., 1994, 2004). This can be illustrated by first detailing the general requirements for good rehabilitation tasks and then examining how they match up with the features that game-based VR provides. To do this, we conjecture seven core requirements for a good rehabilitation task.

The rehabilitation task must be:

- 1. grounded in data-based assessment to specify the target activity to be precisely rehabilitated.
- 2. adjustable in terms of difficulty level from something that is possible for the user to perform, to a level representing the desired end-goal performance.
- 3. capable of repetitive and hierarchical administration to the user.
- 4. quantifiable in order to measure performance and progress.
- 5. capable of providing the user with strategic feedback as to the outcome of performance.
- 6. relevant to real world functional activity.
- 7. capable of motivating user engagement and interaction with the task.

Clinical VR assets are well-matched to meet these requirements, once a rehabilitation objective is specified by state-of-the-art data-based assessment methodologies. VR's capacity for stimulus control (specified earlier in the article) can support the setting of a baseline challenge level that the user is capable of accomplishing. The stimulus control asset can also leverage the tireless capacity of the computer to generate the repetitive and hierarchical delivery of stimulus challenges across a range of programmable difficulty levels. In this way, an individual's rehabilitation activity can be customized to begin at a stimulus challenge level attainable and comfortable for them, with gradual titration to higher or lower difficulty levels based on user performance. The interaction between the user's behavior and task demands can be automatically scored by the VR software to measure performance, and provide real-time strategic feedback that can be automatically administered as needed to shape and modulate performance toward a successful goal. All of this can occur within simulated VR contexts that embody the *complex functional challenges* that exist in everyday ecologically-relevant settings. Thus, the experimental control required for rigorous scientific measurement, analysis, and replication can still be maintained while the user is presented with challenges that require real-world functional behaviors.

At each step in this process, computer game development principles and evidencebased rehabilitation task design (Lange et al., 2009, 2010; 2012), can be combined to promote user motivation and engagement. The VR assets described here follow the same structure for good computer game design. For example, to maintain motivation, game designers develop content that provides challenges within what is called the "flow channel". Schell (2014) details the flow channel, derived from Csikszentmihályi (1990), as, "...the narrow margin of challenge that lies between boredom and frustration, for both of these unpleasant extremes cause our mind to change its focus to a new activity." (pp. 119). By integrating such game development principles with Clinical VRs capacity to deliver systematically controllable simulations, it is now possible to create compelling rehabilitation tasks to enhance client motivation and engagement beyond what may be possible with other existing methodologies. The feasibility of translating traditional evidence-based interventions into computer gaming formats is increasingly being recognized by clinicians and scientists as a methodology for exploiting the features of games for therapeutic change (Fleming et al., 2016). Moreover, the growing recognition of the potential value of gamification (and the need for more research) in healthcare and the field of "Games for Health" is evidenced by the appearance of scientific journals and conferences focused on this topic, in addition to an evolving scientific literature. Since a full review of this area is beyond the scope of this

article, the reader is directed to other detailed reviews (Baranowski et al., 2016; Fleming et al., 2016; Granic et al., 2014; Kato, 2010; Papastergiou, 2009).

Beyond efficacy: VR as a tool for breaking down barriers to care

This final asset is really a more speculative discussion of how VR at the current time may have value beyond improving the efficacy of a clinical process and rather, is more concerned with how VR could serve to break down some barriers to care. It is included here since some of these factors may serve to inform later judgments as to Clinical VR's readiness for improving clinical practice and research. The main premise here is that the best evidence-based approach for assessing or treating a clinical health condition serves little value if clients do not seek it out and participate in it. There are many reasons why these barriers limit client access to care and more detail can be found in (Andrade et al., 2015; Clement et al., 2015). To more readily consider these barriers, we have constructed an intuitive model for detailing them, called the 7A's. The 7A's stand for: Awareness, Anticipated Benefit, Access, Availability of well-trained providers, Acceptability for seeking treatment, Adherence, and Affordability.

Clinical VR may be strategically well-placed to break down some (but not all) of the barriers that keep people from receiving the benefits of clinical care. To start, client awareness of the range of available evidence-based treatment options may be limited. Perhaps some remedy for this exists in the media exposure that is currently at an all-time high for VR. In addition to the media excitement and interest in novel efforts to use VR for gaming and entertainment purposes, there has also been significant coverage of VR healthcare applications. This may be in part due to a desire in some quarters of popular culture to promote VR's image as useful for pro-social purposes, beyond first person shooter games. Thus, a quick search of the internet will uncover a large volume of "heartstring tugging" media reports on VR's application with clinical conditions, especially those that are at the forefront of the public consciousness (e.g., PTSD, Autism, Stroke, Alzheimer's, Depression, Opiate Addiction, etc.). For better or worse, and in spite of the occasional scientific and factual errors in the popular press, there is no doubt that Clinical VR applications have received significant media visibility. Whether this builds public awareness of treatment options that leads to actual help-seeking is still an open question in need of more research.

As well, the double-edged sword of media claims about *anticipated benefit* can be problematic. The balance between over-wrought claims of clinical success and actual data points can sometimes err on the side of higher-than-warranted expectations. However, when a Clinical VR research study does provide positive evidence, the popular media's focus on covering that finding is fairly certain, thus reaching the eyes and ears of people who will hopefully seek help, either for themselves or a loved one. For example, our PTSD VR exposure work has garnered significant popular media reporting that is typically followed by an uptick in client or family member queries as to where treatment can be accessed. The perception of the "sexiness" of the use of "exotic" VR technology in the popular culture may also build expectations of success that in the end may drive a stronger placebo effect in those who undergo VR-based services.

Making treatment more *accessible*, is a factor for people who live in remote locations or who face transportation challenges, and has served to drive efforts at using teletherapy or online self-help CBT programming. However, as stated in the "independent practice" section, VR as a tool for pushing care outside of the clinic is still limited by cost and complexity issues, as well as by ethical concerns. This may be less limited in the future with the growing availability of low-cost VR technology in the home, but for now, Clinical VR is not seen to reduce the impact of this barrier. Similarly, the *availability* of well-trained providers

who are properly trained in Clinical VR procedures is still limited. While many VR approaches follow the procedures and mechanics of traditional forms of therapy (e.g., VR exposure therapy for anxiety disorders uses the same treatment protocol endorsed for imaginal exposure approaches), the operation of VR equipment does require some specialized training. This training is becoming more available either from standalone workshops or CME offerings at respected conferences, but it is not commonplace at the current time. However, the use of VH patients for training novice clinicians (Talbot et al., 2012; Rizzo et al., 2011, 2016a) is an emerging area of focus, and this may have a direct impact on improving clinical use and supporting the greater availability of well-trained providers.

The *acceptability* of seeking care can be improved by reducing the internal or external perceptions of stigma that a potential client may feel when admitting that they have a problem. Although this may be less relevant for those seeking help to address a CNSrelated condition, it is often a factor that limits help-seeking for those with psychological health conditions. This is an area where Clinical VR has some early research support. In a survey study to assess openness to seeking care in 325 active duty Army SMs (Wilson et al., 2008), results indicated that 83% of the participants reported that they were neutral-tovery-willing to use some technology as part of a treatment; 71% were equally willing or more willing to use a treatment based on technology than to talk to a therapist in a traditional treatment setting. Moreover 20% of SMs, who stated they were not willing to seek traditional psychotherapy, rated their willingness to use a VR-based treatment as neutral to very willing. One possible interpretation of this finding is that a subgroup of this sample of SMs with a significant disinterest in traditional mental health treatment would be willing to pursue treatment with a VR-based approach. Thus, VR exposure therapy may offer an appealing treatment option for "digital generation" SMs and Veterans who may be reluctant to seek out what they perceive as traditional talk therapies. Other research using VR exposure for PTSD and phobias with civilian groups has shown high levels of treatment satisfaction with VR (Banos et al., 2009; Beck et al., 2007;) and in some reports, participants reported that it was easier to take the first step in confronting fears with VR compared imaginal exposure. Certainly, more research is needed to determine whether Clinical VR approaches reduce stigma and promote help-seeking. However, one can speculate that younger groups who have grown up in this "digital age" may actually be more attracted to and comfortable with participation in a Clinical VR approach and this could be a factor for reducing stigma and increasing the acceptability of VR-based care.

Finally, more research is needed to investigate the impact of Clinical VR for promoting *adherence* to a full course of treatment. Although a number of small studies have suggested a higher positive interest in continuing treatment with VR (cf. Bryanton et al., 2006), most research examining treatment adherence as a specific variable has been underpowered. While the motivating factors of Clinical VR tools are frequently referred to in the literature, we are not aware of any systematic evaluations of VR treatment characteristics and their impact on patient attrition for prolonged, repetitive treatment protocols. We expect factors such as multiplayer and competitive training content, level of immersion, story-driven/narrated treatment content, or relevance of treatment content to the patient's everyday life to be important factors for sustained patient motivation. The relevance of the aforementioned "flow channel" (Schell, 2014) and its impact on user motivation and engagement cannot be overstated. Thus, bridging the gap between scientific construction of evidence-based treatment tasks and artistic design of game-based content seems a worthwhile target for further investigation.

Affordability has also been an issue that has limited VR treatment access in the past. This is expected to be less of a limiting factor, now that higher fidelity, yet low-cost systems have come onto the market. As a point of comparison, it is now possible to purchase a high-fidelity VR HMD for \$800 (HTC Corporation, 2017) that has superior

specifications compared to a system that would have cost \$20,000 (NVIS Inc, 2017) to purchase 5 years ago. In addition, low-cost smartphone-based VR HMDs are likely to achieve parity with computer-tethered systems for some Clinical VR applications and this is predicted to dramatically reduce hardware costs and improve affordability. With large technology companies such as Facebook, Google, Apple, and Samsung invested in the VR market, we anticipate new and affordable hardware and software to be released more frequently over the next few years. Moreover, successful companies in the Clinical VR space (e.g. MindMaze, SilverFit, Gesturetek Health) are paving the way for a competitive landscape of VR tools for clinical assessment and treatment that will inevitably result in more affordable options for researchers and clinical providers. As these companies continue their R&D work on innovative VR applications, we hope to see diversity and accessibility in this growing market, not unlike Google's Play Store or Apple's App Store, again with the result of more affordable prices for clinical end-users and eventually for home-based use by patients.

Discussion – Is Clinical Virtual Reality Ready for Primetime?

The question of Clinical VR's readiness for widespread clinical use can be considered across the criteria of *theory, research, pragmatics*, and *ethics*. On the basis of the clear assets and features that are available with simulation technology, there is a sound *theoretical* basis for the development and implementation of informed Clinical VR applications. General simulation technology has a long history of adding value in aviation simulation, military planning, automotive/aircraft design, and surgical planning (Virtual Reality Society, 2017). By leveraging these same assets, but in a form factor that can deliver VR experiences within a clinicians' office or research laboratory, a new set of virtual tools become possible for psychology and rehabilitation. While any given Clinical VR application will likely not leverage all of the VR assets described in this article, a clear specification of what features can be brought to bear on a clinical target is recommended to guide design, implementation, and evaluation in a systematic fashion.

A guiding principle in our work is to first look at known processes operating in physical reality that are believed to contribute to the creation of an evidence-based approach to assessment and intervention. With that as a starting point, one can specify the VR assets that can underlie and guide the creation of a VR application to: provide more reliable and valid assessments, amplify treatment effects, break down barriers to care, or simply reduce costs by automating processes. For example, we know that the use of imaginal exposure approaches for anxiety disorders are evidence-based in the physical world. From that, one can see a direct case for using VR to deliver ecologically relevant simulations, within which we can precisely control and titrate the delivery of progressively more provocative stimuli to pace exposure for the end goal of promoting extinction learning. Similarly, we know that the sheer amount of physical rehabilitation activity that a stroke survivor engages in (all other factors being equal) is related to improved outcomes. From that, it is logical to hypothesize that if compelling game-based VR rehabilitation tasks are developed, it may be possible to motivate users to do more repetitions, leading to improved outcomes. These thumbnail examples simply present one or two of the assets that can inform the rationale for Clinical VR use cases, but in reality, there may be any number of additional features that can be specified and marshalled (e.g., strategic feedback, cueing stimuli, safety, etc.) for adding value over existing traditional methods. Thus, it is our perspective that the theoretical basis for using Clinical VR is sound and supportive of its "primetime" application.

The *research* support for the use of Clinical VR is promising, albeit not fully mature. There seems to be a consensus in the literature, that VR can produce equivalent or better outcomes for exposure-based approaches for anxiety disorder treatment (e.g., Bouchard et al., 2017; Maples-Keller et al., 2017; Morina et al., 2015; Rizzo et al., 2015a). Consistent findings have also been produced in support of VR as an effective distraction tool for reducing the perception of pain in patients undergoing acutely painful medical procedures (e.g. Hoffman et al., 2011; Trost et al., 2015). A growing body of research is indicating that VR can increase participation in physical rehabilitation, with patients reporting more motivation to engage in rehab tasks within a game-based VR context compared to standalone training (e.g. Granic et al., 2014). Cognitive assessment methods using VR have produced promising results in construct validation studies, and for distinguishing between clinical groups and healthy controls (e.g. Man et al., 2016; Nir-Hadad et al., 2015; Parsons & Rizzo, 2008b; Rizzo et al., 2006). And finally, the use of Virtual Humans in Clinical VR applications has produced promising results indicating that they can foster credible interactions with real people for training, as healthcare guides, and in the role of clinical assessors, but this area is still in a very early state of maturity (Rizzo et al., 2015b, 2016ab; Scherer et al., 2014; Talbot et al., 2012). By contrast, whether due to the complexity of the problem space or the lack of standards in VR research methodology, cognitive rehabilitation studies using VR interventions have provided more mixed outcomes. Again, there is consensus about the promise of VR cognitive rehabilitation tools (e.g. Bogdanova, Yee, Ho, & Cicerone, 2016; Ogourtsova, Silva, Archambault, & Lamontagne; 2015; Valladares-Rodriguez et al., 2016), but the majority of conducted studies are pilot trials without sufficient power or the study design needed to draw decisive conclusions about efficacy, transfer of gained skills to the daily life of clients, long-term outcomes, and cost-effectiveness.

A continued focus on research methodology, selection of outcome measures, quantification of training transfer to daily life, and the identification of "active ingredients" of Clinical VR tools is needed to advance its thoughtful and scientifically valid use. This includes answering questions about: the frequency and modality of feedback and cues; treatment doses and frequencies; complexity of VR tasks and environments; importance of graphical realism and fidelity; selection and usability of interface devices; relevance of gamification and multiplayer/competitive elements; and many other factors that inform VR system design. Importantly, these questions need to be posed for each of the diverse patient populations that stand to benefit from Clinical VR tools. In sum, the research is generally supportive for the "primetime" use of Clinical VR in some areas, but there should be no illusion as to the need for more research investigating the boundary conditions for its safe and effective application.

The positive outcomes seen in the Clinical VR literature thus far are actually quite encouraging when viewed in the context of the challenges that researchers faced in these areas. First, the general availability of the technology has only existed for about 25 years and for the first 10-15 years of that, the maturity of the hardware and software was guite variable. During those early years, with the notable exception of exposure therapy applications, Clinical VR R&D was essentially exploratory, primarily characterized by one-off, proof-of-concept, prototype systems. While these systems produced interesting results in uncontrolled, small sample size studies, only a few applications were subjected to rigorous parametric tests by independent researchers. As a result, most Clinical VR review articles include the staple recommendation that, "while current VR findings are promising, more controlled research with larger sample sizes are needed.". This is not a slight on innovative researchers who had to bear the double burden of acquiring funding for both system development and clinical tests, with a technology that was sometimes perceived by grant reviewers as being too "science-fiction-y" to support good science! Rather, it is just an observation on the challenges that have slowed the progression of tightly controlled research in some Clinical VR areas. Thus, when one considers that psychology as a science has been around for about 125 years with a focus on studying human behavior and interaction in the physical world, it makes sense that we may need a few more years to evolve the science for how humans behave and interact in the virtual world.

By contrast, the *pragmatics* for developing and using Clinical VR systems are quite favorable. Over the last 10 years, the technology has gradually advanced enough to support

widespread VR system development beyond what was only possible within very specialized research institutes. This has now been recognized by the Gartner Group (2016) with their elevation of VR from the "trough of disillusionment" to the "slope of enlightenment" in the Hype Cycle for Emerging Technologies. A key factor for VR's recent expansion is a growing VR development community that thrives on access to affordable design tools and VR hardware. Development software (e.g. game engines Unity3D, Unreal Engine, Amazon *Lumberyard*) has seen a large boost in popularity over the past five years and has even found its way into high school and college computer science curriculums. Any interested student, educator, hobbyist, or entrepreneur can pick up these tools for free and begin developing VR applications without much upfront investment or any of the barriers that VR R&D teams faced in the past. We expect this momentum and growth of the VR developer community to translate to a surge of new VR applications, including Clinical VR tools. The online PC distribution platform and community Steam (Valve Corporation, 2017) is currently listing more than 1900 VR-enabled PC games. We anticipate similar distribution platforms to emerge for Clinical VR content that will provide greater access to affordable libraries of archetypic treatment and assessment scenarios for healthcare providers and researchers.

As we look to the future, we see Clinical VR as one of the larger domains of general VR usage. In the recent Goldman Sachs (2016) market analysis looking at the future of VR in 2025, we of course see that Gaming and Entertainment garners the largest market share. While this is to be expected with the public's chronic demand for new and better ways to consume media, the little noticed item in that market analysis is that "healthcare" comes in second for the VR market share. This is not a surprise to researchers and clinicians who have worked in this area over the years, especially as we see healthcare costs becoming one of the largest line items in the US Govt. budget, after Defense. Interest in Clinical VR by actual therapists also seems to be substantial. Norcross et al. (2013) surveyed 70 psychotherapy experts regarding interventions they predicted to increase in the next decade and VR was ranked 4th out of 45 options with other computer-supported methods occupying 4 out of the top 5 positions.

The *ethical* use of VR needs to be considered thoughtfully in any assessment of its future primetime impact on psychological practice or science. Current VR technology now allows for the creation of emotionally evocative virtual experiences. With Clinical VR, we often aim to leverage that capability for a positive impact in client care. But if we accept that it is possible to create experiences that can evoke strong emotions for a positive clinical purpose, we must also accept the probability of some risks for the occurrence of unforeseen negative emotional reactions. Thus, the question of safe and ethical use of VR has been addressed in detail at various junctures (Madary & Metzinger, 2016; Rizzo, Schultheis, & Rothbaum, 2003; Yellowlees, Holloway, & Parish, 2012; Tart, 1993). While there are a variety of ethical issues for the general application of VR beyond its clinical use (e.g. motion sickness side effects, overuse, violent content, etc.), our focus here is limited to the use of VR as a tool for clinical diagnosis and treatment.

Thus far, a significant literature has emerged in support of the positive impact of welldesigned, theory-informed VR applications on mental health and physical functioning. These applications are typically administered within the controlled and safe context of the therapy setting, supervised by a well-trained clinician. However, what happens if these types of VR experiences become commodity products that are readily accessible to anyone who selfdiagnoses their clinical condition and then uses VR treatment content as a "self-help" therapy? While some might say this is not much different than purchasing a self-help book and following the instructions and recommendations therein, VR experiences may have more impact on a user than what may occur from reading a book. Similar to most areas of mental health care, there is also a risk that this form of self-diagnosis and treatment is based on inaccurate or counterproductive information. Another kind of ethical challenge can also emerge if a clinician decides that VR would be great for generating a buzz for their practice and result in more business, but the clinician hasn't had sufficient training in its use and safe application. Thus, there are issues of concern here from the perspective of patients and providers. Consequently, there is a need for ethical guidelines regarding the safe and informed use of Clinical VR applications, much like the way that pharmaceutical treatments are managed by a well-trained and qualified physician.

In the area of clinical practice, the American Psychological Association's ethical code provides a clear and well-endorsed set of guidelines that can serve as a good starting point for understanding and proactively addressing some of the basic issues for the creation and use of VR applications in clinical practice (APA, 2003). Three core areas of clinical practice concerns and recommendations can be derived from these guidelines (two of which come directly from the APA code):

1. "2.01 Boundaries of Competence

(a) Psychologists provide services, teach and conduct research with populations and in areas only within the boundaries of their competence, based on their education, training, supervised experience, consultation, study or professional experience."

Recommendation: VR-delivered mental health assessment/treatment may require fundamentally different skill sets than what is needed for traditional "talk therapy" approaches. Clinicians need to have specialized training, and possibly in the future, some level of certification in the safe and ethical use of VR for therapy.

2. "2.04 Bases for Scientific and Professional Judgments

Psychologists' work is based upon established scientific and professional knowledge of the discipline."

Recommendation: VR applications that are developed for clinical assessment and treatment must be based on a theoretical framework and documented with some level of research before they can be endorsed as evidence-based and marketed as such. In an emerging area like VR where unique and specific guidelines have yet to be established, the practitioner must be fully transparent about the evidence base for the approach and take precautions to preserve the safety and integrity of the patient.

3. Self-Diagnosis / Self-Treatment

While not cited as an APA standard, the issues regarding patient self-diagnosis and selftreatment deserve further mention. Mental health conditions can be extremely complex and in some instances the self-awareness of the patient may be compromised. This can oftentimes lead to a faulty self-diagnosis as well as the problems that arise when the patient searches for symptom information on the internet where reliable and valid content can be questionable. The same issues come into play with self-treatment. The problems that can ensue are two-fold.

a. The patient makes errors in either or both areas and achieves no clinical benefit, or worse, aggravates the existing condition with an ineffective or inappropriate VR approach that actually does more harm.

b. By pursuing a "seductive" VR self-help approach that is misaligned with their actual needs or has no evidence for its efficacy, the patient could miss the opportunity to receive quality evidence-based care that is designed and delivered based on the informed judgment of a trained expert diagnostician or clinical care provider.

These two negative impacts could occur if a company produces a VR approach without sufficient validation and markets it to the public as a valid test or cure. This has been seen over the years with many forms of quack medicine and there needs to be some principle about the promotion of a VR application that has the consumer's protection in mind. This issue is particularly important at the current time in view of all the public exposure, hype, and genuine excitement surrounding VR. There are many new companies emerging in the healthcare space, essentially being driven by venture capitalists and game developers, without any credible expert clinical and/or research guidance. Such companies could not only do harm to users, but the uninformed development and over-hype of the benefits to be derived from a VR clinical application leading to negative effects could serve to create the general impression that VR is a "snake oil" approach and lead to people *not* seeking (or benefiting from) an otherwise well-validated VR approach.

An example of a "grey area" in this domain concerns one of the most common fears that people report - public speaking. Technically, in an extreme form where it significantly impairs social and occupational functioning, public speaking anxiety would qualify as a phobia and be diagnosed as an anxiety disorder. However, since most people do have some level of sub-clinical fear of public speaking (that they eventually get over with practice), this has been one of the first areas where widespread consumer access to Public Speaking VR exposure therapy software has occurred (Hypergrid Business, 2016). Users can practice their presentation "skills" on a low-cost smartphone-based VR HMD (e.g. Google Cardboard/Daydream, Samsung Gear VR) in front of various types of audiences and settings. In this case, most clinicians would not show much concern for this type of self-help skills training approach and the potential for damaging effects to a user appears to be fairly minimal. But, from this example, can we now expect that applications will be made readily available for other and perhaps more complex anxiety disorder-based phobias (Fear of Flving, Social phobia, Driving, Spiders, Intimacy, etc.), or even for PTSD treatment? Consequently, it appears that ethical guidelines may be needed to support the safe use of Clinical VR.

In conclusion, interest in the clinical uses of VR technology has accelerated and will likely continue to be fueled by a societal zeitgeist in which this form of immersive and interactive technology inspires the public's attention and imagination. While previously hamstrung by costs, complexity, and clinician unfamiliarity with VR equipment, the technology has evolved dramatically in the consumer marketplace with new low-cost, hi-fidelity, product offerings that are poised to drive wider scale adoption. This will result in a probable future scenario where VR devices will become like toasters—although you may not use it every day, every household will have one. When such market penetration occurs, the general public will have more access to a range of VR experiences. This may serve to accelerate the uptake of Clinical VR as users, more familiar with the technology, begin to imagine its value beyond the world of digital games.

The momentum generated by the growing public awareness of VR coupled with advances in the technology has created a unique opportunity for psychology and rehabilitation. Our analysis of the theoretical underpinnings and research findings to date leads us to predict that the application of Clinical VR will have a significant impact on future research and practice. The pragmatic issues that may influence its adoption as a tool across many areas of psychology also appear favorable, but professional guidelines will be needed to promote its safe and ethical use. Such guidelines should inform the development of principles for Clinical VR application design, distribution, practice, and training. While there is still much work to be done to advance the science in this area, we strongly believe that Clinical VR applications will become indispensable tools in the toolbox of psychological researchers and practitioners and will only grow in relevance and popularity in the future. Thus, it is our assessment that Clinical VR is indeed ready for primetime!

For access to a large library of online videos demonstrating many of the applications discussed here, go to: <u>https://www.youtube.com/user/albertskiprizzo</u>

References

Adamovich, S. V., Fluet, G. G., Tunik, E., & Merians, A. S. (2009). Sensorimotor training in virtual reality: a review. *NeuroRehabilitation*, *25*(1), 29-44.

Akinwuntan, A.E., Wachtel, J., & Rosen, P.N. (2012). Driving Simulation for Evaluation and Rehabilitation of Driving After Stroke. *Journal of Stroke and Cerebrovascular Diseases*, *21(6)*, 478-486.

Albright, G., Adam, C., Serri, D., Bleeker, S., & Goldman, R. (2016). Harnessing the power of conversations with virtual humans to change health behaviors. *mHealth*, 2(11).

American Psychological Association (2003). *Ethical Principles of Psychologists and Code of Conduct.* Retrieved from http://www.apa.org/ethics/code/.

Anderson, P.L., Zimand, E., Hodges, L.F., & Rothbaum, B.O. (2005). Cognitive behavioral therapy for public-speaking anxiety using virtual reality for exposure. *Depression and Anxiety*. 22(3), 156-158.

Andrade, L.H., Alonso, J., Mneimneh, Z., Wells, J.E., Al-Hamzawi, A., et al. (2015). Barriers to Mental Health Treatment: Results from the WHO World Mental Health (WMH) Surveys. *Psychol Med*, *44*(*6*), 1303–1317. doi: 10.1017/S0033291713001943

Astur, R.S., Oriz, M.L. & Sutherland, R.J., (1998). The characterization of performance by men and women in a virtual Morris water task: A large and reliable sex difference. *Behavioral Brain Research*, 93, 185-190.

Astur, R. S., St. Germain, S. A., Tolin, D., Ford, J., Russell, D., & Stevens, M. (2006). Hippocampus function predicts severity of post-traumatic stress disorder. *Cyberpsychology* & *Behavior*, *9*(2), 234-240.

Astur, R.S., Taylor, L.B., Mamelak, A.N., Philpott, L. and Sutherland, R.J. (2002). Humans with hippocampus damage display severe spatial memory impairments in a virtual Morris water task. *Behavioural Brain Research*, 132, 77-84.

Astur, R.S., Tropp, J., Sava, S., Constable, R.T., and Markus, E.T. (2004). Sex differences in a virtual Morris water task and a virtual eight-arm maze. *Behavioural Brain Research*. 151(1-2):103-15.

Aukstakalnis, & Blatner, D. (1992). *Silicon Mirage: The Art and Science of Virtual Reality.* Peachpit Press, Berkeley, CA, USA.

Badia, S. B., Fluet, G. G., Llorens, R., & Deutsch, J. E. (2016). Virtual reality for sensorimotor rehabilitation post stroke: Design principles and evidence. In *Neurorehabilitation Technology* (pp. 573-603). Springer International Publishing. Cham, Switzerland.

Bailenson, J.N. & Beall, A.C. (2006). Transformed social interaction: Exploring the digital plasticity of avatars. In Schroeder, R. & Axelsson, A.'s (Eds.), *Avatars at Work and Play: Collaboration and Interaction in Shared Virtual Environments*, 1-16, Springer-Verlag, Berlin, Germany,

Baños, R.M., Botella, C., Guillen, V., García-Palacios, A., Quero, S., Bretón-López, J., & Alcañiz, M. (2009). An adaptive display to treat stress-related disorders: EMMA's world. *British Journal of Guidance and Counseling*, *37*(3), 347–356.

Baños, R.M., Guillen, V., Quero, S., García-Palacios, A., Alcaniz, M. & Botella, C. (2011). A virtual reality system for the treatment of stress-related disorders: A preliminary analysis of efficacy compared to a standard cognitive behavioral program. *International Journal of Human Computer Studies, 69*(9), 602–613.

Baranowski, T., Blumberg, F., Buday, R., DeSmet, A., Fiellin, L. E., Green, C. S., ... & Morrill, B. A. (2016). Games for health for children—Current status and needed research. *Games for health journal*, *5*(1), 1-12. Downloaded from: http://www.icdvrat.org/2016/papers/ICDVRAT2016_S02N2_Bresnahan_etal.pdf

Barrett, J., McCrindle, R.J., Cook, G.K., Booy, D.A. (2002). Accessible interface design: A review of access to information and communication technology for older and disabled people. Technical Report, available from Department of Computer Science, The University of Reading.

Beck, A.T., Epstein, N., Brown, G. and Steer, R.A. (1988). An inventory for measuring clinical anxiety: psychometric properties *Journal of Consulting and Clinical Psychology*, *56*, 893-897.

Beck, J.G., Palyo, S.A., Winer, E.H., Schwagler, B.E., & Ang, E.J. (2007). Virtual reality exposure therapy for PTSD symptoms after a road accident: an uncontrolled case series. *Behavior Therapy*, 38(1), 39–48.

Beidel, D. C., Frueh, B. C., Neer, S. M., & Lejuez, C. W. (2017). The efficacy of Trauma Management Therapy: A controlled pilot investigation of a three-week intensive outpatient program for combat-related PTSD. *Journal of Anxiety Disorders*, *50*, 23-32.

Bickmore, T. W., Utami, D., Matsuyama, R., & Paasche-Orlow, M. K. (2016). Improving access to online health information with conversational agents: a randomized controlled experiment. *Journal of medical Internet research*, *18*(1).

Blascovich, J., Loomis, J., Beall, A., Swinth, K., Hoyt, C., & Bailenson, J. (2002). Immersive virtual environment technology: Not just another research tool for social psychology. *Psychological Inquiry*, 13, 103-124.

Blume, F., Hudak, J., Dresler, T., Ehlis, A. C., Kuhnhausen, J., Renner, T. J., & Gawrilow, C. (2017). NIRS-based neurofeedback training in a virtual reality classroom for children with attention-deficit/hyperactivity disorder: study protocol for a randomized controlled trial. *Trials*, *18*(1), 41. doi:10.1186/s13063-016-1769-3

Bogdanova, Y., Yee, M.K., Ho, V.T., & Cicerone, K.D. (2016). Computerized Cognitive Rehabilitation of Attention and Executive Function in Acquired Brain Injury: A Systematic Review. *J Head Trauma Rehabil* 31(6), 419-433.

Bohil, C. J., Alicea, B., & Biocca, F. A. (2011). Virtual reality in neuroscience research and therapy. *Nature Reviews Neuroscience*, *12*(12), 752-762.

Bordnick, P.S., Yoon, J.H., Kaganoff, E., & Carter B. (2013). Virtual Reality Cue Reactivity Assessment A Comparison of Treatment-vs. Nontreatment-Seeking Smokers. *Research on Social Work Practice*, 23(4), 419-425.

Botella, C., Serrano, B., Baños, R. M. & Garcia–Palacios, A. (2015). Virtual reality exposurebased therapy for the treatment of post-traumatic stress disorder: a review of its efficacy, the adequacy of the treatment protocol, and its acceptability. *Neuropsychiatric Disease and Treatment*, 11, 2533–2545.

Bouchard, S., Dumoulin, S., Robillard, G., Guitard, T., Klinger, E., Forget, H., Loranger, C., & Roucaut, F.X. (2017). Virtual reality compared with *in vivo* exposure in the treatment of social anxiety disorder: a three-arm randomised controlled trial. *The British Journal of Psychiatry*, *210*(*4*), 276-283. DOI: 10.1192/bjp.bp.116.184234.

Bresnahan, T., Rizzo, A.A., Burke, S.L., Partin, M., Ahlness, R.M., & Trimmer, M. (2016). Using Virtual Interactive Training Agents (VITA) with Adults with Autism and other Developmental Disabilities. In *The 2016 Proceedings of the International Conference on Disability, Virtual Reality and Associated Technologies*. Available at:

Brooks, B.M., McNeil, J.E., Rose, F.D., Greenwood, R.J., Attree, E.A. and Leadbetter, A.G. (1999). Route learning in a case of amnesia: A preliminary investigation into the efficacy of training in a virtual environment. *Neuropsychological Rehabilitation*, *9*, 63-76.

Brown, D. J., Kerr, S. J., and Bayon, V. (1998). The development of the Virtual City: A user centred approach. In Sharkey, P., Rose, D. and Lindstrom, J. (Eds.), Proceedings of the 2nd European Conference on Disability, Virtual Reality and Associated Technologies (ECDVRAT). Reading UK: University of Reading. 11-16.

Burgers, C., Eden, A., van Engelenburg, M., & Buningh, S. (2015). How feedback boosts motivation and play in a brain-training game. *Computers in Human Behavior, 48,* 94-103.

Bryanton, C., Bosse, J., Brien, M., Mclean, J., McCormick, A., & Sveistrup, H. (2006). Feasibility, motivation, and selective motor control: virtual reality compared to conventional home exercise in children with cerebral palsy. *Cyberpsychology & behavior*, *9*(2), 123-128.

Carlbring, P., Westling, B.E., Ljungstrand, P., Ekselius, L., & Andersson, G. (2001). Treatment of Panic Disorder Via the Internet: A Randomized Trial of a Self-Help Program. *Behavior Therapy, 32*, 751-764.

Casutt, G., Martin, M., Keller, M., & Jäncke, L. (2014). The relation between performance in on-road driving, cognitive screening and driving simulator in older healthy drivers. *Transportation Research Part F, 22*, 232-244.

Chirico, A., Lucidi, F., de Laurentiis, M., Milanese, C., Napoli, A., & Giordano, A. Virtual Reality in Health System: Beyond Entertainment. A Mini-Review on the Efficacy of VR During Cancer Treatment. *J Cell Physiol, 231*, 275-287. DOI: 10.1002/jcp.25117.

Chou, Y. H., Weingarten, C. P., Madden, D. J., Song, A. W., & Chen, N. K. (2012). Applications of virtual reality technology in brain imaging studies. In *Virtual Reality in Psychological, Medical and Pedagogical Applications*. InTech.

Clement, S., Schauman, O., Graham, T., Maggioni, F., Evans-Lacko, S., et al. (2015). What is the impact of mental health-related stigma on help-seeking? A systematic review of quantitative and qualitative studies. *Psychol Med, 45(1)*, 11–27. https://doi.org/10.1017/S0033291714000129 Christiansen, C., Abreu, B., Ottenbacher, K., Huffman, K., Massel, B., & Culpepper, R. (1998) Task performance in virtual environments used for cognitive rehabilitation after traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 79*, 888-892. Connor, B. Wing, A.M., Humphreys, G.W., Bracewell, R.M. & Harvey, D.A. (2002). Errorless Learning Using Haptic Guidance: Research in Cognitive Rehabilitation Following Stroke. In Sharkey, P. Lanyi, C.S. & Standen, P. (Eds.), *Proceedings of the 4th International Conference on Disability, Virtual Reality, and Associated Technology*. Reading, UK: University of Reading, 77-86.

Costanzo, M.E, Leaman, S., Jovanovic, T., Norrholm, S.D., Rizzo, A.A., Taylor, P., & Roy, M.J. (2014). Psychophysiological Response to Virtual Reality and Sub-threshold PTSD Symptoms in Recently Deployed Military. *Psychosomatic Medicine*, *76*(9), 670-677.

Costas, R., Carvalho, L. & de Aragon, D. (2000). Virtual city for cognitive rehabilitation. In Sharkey, P., Cesarani, A., Pugnetti, L. & Rizzo, A. (Eds.), *Proceedings of the 3rd International Conference on Disability, Virtual Reality, and Associated Technology* (pp. 305-313). Reading, UK: University of Reading.

Cox, S.M., Cox, D.J., Kofler, M.J., Moncrief, M.A., Johnson, R.J., et. al. (2015). Driving Simulator Performance in Novice Drivers with Autism Spectrum Disorder: The Role of Executive Functions and Basic Motor Skills. *J Autism Dev Disord*, DOI 10.1007/s10803-015-2677-1.

Cromby, J., Standen, P., Newman, J., Tasker, H. (1996). Successful transfer to the real world of skills practiced in a virtual environment by student with severe learning disabilities. In: Sharkey, P.M. (Ed) *Proceedings of the 1st European Conference on Disability, Virtual Reality and Associated Technologies*. Reading, UK: University of Reading, 305-313.

Cruz-Neira C., Sandin D. J., DeFanti T. A. (1993). Surround-screen projection-based virtual reality: the design and implementation of the CAVE. Proc. 20th Annual Conf. on Computer Graphics and Interactive Techniques, 135–142, New York, NY: ACM.

Csikszentmihályi, M. (1990). Flow: The Psychology of Optimal Experience. Harper & Row.

Cuijpers, P., van Straten, A., & Andersson, G. (2008). Internet-administered cognitive behavior therapy for health problems: a systematic review. *J Behav Med*, *31*, 169–177.

Darejeh, A. & Singh, D. (2013). A review on user interface design principles to increase software usability for users with less computer literacy. *Journal of Computer Science*, *9*(*11*), 1443-1450. doi:10.3844/jcssp.2013.1443.1450.

Dascal, J., Reid, M., IsHak, W. W., Spiegel, B., Recacho, J., Rosen, B., & Danovitch, I. (2017). Virtual reality and medical inpatients: A systematic review of randomized, controlled trials. *Innovations in clinical neuroscience*, *14*(1-2), 14.

Davies, R. C., Johansson, G., Boschian, K, Lindén, A., Minör, U., & Sonesson, B. (1998). A practical example using virtual reality in the assessment of brain injury. In Sharkey, P., Rose, D. & Lindstrom, J. (Eds.), *Proceedings of the 2nd European Conference on Disability, Virtual Reality and Associated Techniques.* Reading UK: University of Reading, 61-68.

Davis, E.S. & Wachtel, J, (2000). *Interactive Driving Simulation as a Tool for Insight Development and Motivation in a Rehabilitation Setting.* . Paper presented at the 8th Annual Medicine Meets Virtual Reality Conference, Newport Beach, CA. January 22, 2000.

DeFanti, T.A., Acevedo, D., Ainsworth, R.A., Brown, M.D., Cutchin S., et al. (2011). The Future of the CAVE. *Cent. Eur. J. Eng.*, *1*(*1*), 16-37. doi: 10.2478/s13531-010-0002-5.

Deutsch, J.E., Latonio, J., Burdea, G. & Boian, R. (2001) Post-Stroke rehabilitation with the Rutgers Ankle System: A Case Study. *Presence: Teleoperators and Virtual Environments*, *10, Presence: Teleoperators and Virtual Environments*, *10,* 416-430.

Deutsch, J. E., & McCoy, S. W. (2017). Virtual Reality and Serious Games in Neurorehabilitation of Children and Adults: Prevention, Plasticity, and Participation. *Pediatric Physical Therapy*, *29*, S23-S36.

DeVault, D., Mell, J., & Gratch, J. (2015, March). Toward natural turn-taking in a virtual human negotiation agent. In S. Andrist, D. Bohus, E. Horvitz, B. Mutlu, & D. Schlangen (Eds.), *AAAI Spring Symposium on Turn-taking and Coordination in Human-Machine Interaction*, (pp. 2-9), Stanford, CA: AAAI Press. Available at: https://www.aaai.org/ocs/index.php/SSS/SSS15/paper/view/10335/10100

Difede, J., Cukor, J., Jayasinghe, N., Patt, I., Jedel, S., Spielman, L., et al. (2007). Virtual Reality exposure therapy for the treatment of posttraumatic stress disorder following September 11, 2001. *Journal of Clinical Psychiatry, 68*, 1639-1647.

Difede, J., Cukor, J., Wyka, K., Olden, M., Hoffman, H., Lee, F. S., & Altemus, M. (2014). D-cycloserine augmentation of exposure therapy for post-traumatic stress disorder: a pilot randomized clinical trial. *Neuropsychopharmacology*, *39*(5), 1052-1058.

Elkind, J.S., Rubin, E., Rosenthal, S., Skoff, B. & Prather, P. (2001). A simulated reality scenario compared with the computerized Wisconsin Card Sorting test: An analysis of preliminary results. *Cyberpsychology and Behavior*, *4*, 489-496.

Falconer, C.J., Rovira, A., King, J.A., Gilbert, P., Antley, A., Fearon, P., Ralph, N., Slater, M., & Brewin, C.R. (2016). Embodying self-compassion within virtual reality and its effects on patients with depression. British Journal of Psychiatry Open, 2, 74–80.

Faria, A.L., Andreia, A., Soares, L., & Bermudez i Badia (2016). Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: a randomized controlled trial with stroke patients. *Journal of NeuroEngineering and Rehabilitation, 13:96.* DOI: 10.1186/s12984-016-0204-z

Fish, J. E., Manly, T., Kopelman, M. D., & Morris, R. G. (2015). Errorless learning of prospective memory tasks: An experimental investigation in people with memory disorders. *Neuropsychological rehabilitation*, 25(2), 159-188.

Fleming, T. M., Bavin, L., Stasiak, K., Hermansson-Webb, E., Merry, S. N., Cheek, C., ... & Hetrick, S. (2016). Computer-games for mental health: Current status and promising directions. *Frontiers in Psychiatry*, *7*, 215.

Folley. B.S., Astur, R.S., Jagannathan, K., Calhoun, V.D., Pearlson, G.D. (2010). Anomalous neural circuit function in schizophrenia during a virtual Morris water task. *Neuroimage*, 49(4), 3373-84.

Foloppe, D. A., Richard, P., Yamaguchi, T., Etcharry-Bouyx, F., & Allain, P. (2015). The potential of virtual reality-based training to enhance the functional autonomy of Alzheimer's disease patients in cooking activities: A single case study. *Neuropsychological Rehabilitation*, *25*(1), 1-25.

Freeman, D., Bradley, J., Antley, A., Bourke, E., DeWeevers, N., & Evans, N., et al. (2016). Virtual reality in the treatment of persecutory delusions: randomised controlled experimental study testing how to reduce delusional conviction. *British Journal of Psychiatry, 209*(1):62–67. doi:10.1192/bjp.bp.115.176438

Freeman, D., Reeve, S., Robinson, A., Ehlers, A., Clark, D., Spanlang, B., & Slater, M. (2017). Virtual reality in the assessment, understanding, and treatment of mental health disorders. *Psychological Medicine*, *47*, 1-8. Published online: 22 March 2017 (<u>https://www.cambridge.org/core/journals/psychological-medicine/listing?q=virtual+reality&searchWithinIds=289CD5D69C062986BB9145015E56F0</u> <u>E1</u>).

Gartner Inc. (2016, July 19). Hype Cycle for Emerging Technologies, 2016. Retrieved from http://www.gartner.com/newsroom/id/3412017.

Gamito, P., Oliveira, J., Brito, R., Lopes, P., Rodelo, L., Pinto, L., & Morais, D. (2016). Evaluation of Cognitive Functions through the Systemic Lisbon Battery: Normative Data. *Methods Inf Med,* http://dx.doi.org/10.3414/ME14-02-0021.

Gamito, P., Oliveira, J., Coelho, C., Morais, D., Lopes, P., Pacheco, J., ... & Barata, A. F. (2015). Cognitive training on stroke patients via virtual reality-based serious games. *Disability and rehabilitation*, 39 (4), 385-388.

Gold, J.I., Kim, S.H., Kant, A.J., Joseph, M.H. and Rizzo, A.A. (2006). Effectiveness of Virtual Reality for Pediatric Pain Distraction during IV Placement. *CyberPsychology and Behavior*, 9(2), 207-213.

Goldman-Sachs (January 13, 2016). Virtual and Augmented Reality Understanding the Race for the Next Computing Platform. Available at: <u>http://www.goldmansachs.com/our-</u><u>thinking/pages/technology-driving-innovation-folder/virtual-and-augmented-reality/report.pdf</u>

Granic, I., Lobel, A., & Engels, R. C. (2014). The benefits of playing video games. *American Psychologist*, *69*(1), 66.

Gratch, J. & Marsella, S. (2004). A domain independent framework for modeling emotion. *Journal of Cognitive Systems Research*. *5*(4), 269-306.

Gratch, J., Rickel, J., Andre, E., Cassell, J., Petajan, E., Badler, N. (2002). Creating Interactive Virtual Humans: Some Assembly Required. *IEEE Intelligent Systems*. July/August: 54-61.

Harrison, A., Derwent, G., Enticknap, A., Rose, F.D. & Attree, E.A. (2002). The role of virtual reality technology in the assessment and training of inexperienced powered wheelchair users. *Disability and Rehabilitation, 24,* 599-606.

Hoffman, H. G., Richards, T. L., Bills, A. R., Van Oostrom, T., Magula, J., Seibel, E. J., & Sharar, S. R. (2006). Using fMRI to study the neural correlates of virtual reality analgesia. *CNS spectrums*, *11*(1), 45-51.

Hoffman, H.G., Chambers, G.T., Meyer, W.J., Araceneaux, L.L., Russell, W.J., Seibel, E.J., Richards, T.L. and Sharar, S.R. (2011). Virtual Reality as an Adjunctive Non-pharmacologic Analgesic for Acute Burn Pain During Medical Procedures, *Annals of Behavioral Medicine*. 41(2), 183-191.

Holden, M.K. (2005). Virtual Environments for Motor Rehabilitation: Review. *CyberPsych.* and Behav. 8(3).187-211.

Howard, M. C. (2017). A Meta-Analysis and Systematic Literature Review of Virtual Reality Rehabilitation Programs. *Computers in Human Behavior*. 70, 317-327.

HTC Corporation (2017). HTC Vive. Retrieved from https://www.vive.com.

Hypergrid Business (2016, August 13). 5 VR apps that help you be a better public speaker. Retrieved from http://www.hypergridbusiness.com/2016/08/5-vr-apps-that-help-you-be-a-better-public-speaker/

Innes, M. and Morrison, B. (2017). Projecting the future impact of advanced technologies: Will a robot take my job? *InPsych*, 39(2), Downloaded on June 6, 2017, from: https://www.psychology.org.au/inpsych/2017/april/innes/

Jack, D., Boian, R., Merians, A., Tremaine, M., Burdea, G., Adamovich, S., Recce, M. & Poizner, H. (2001). Virtual Reality-Enhanced Stroke Rehabilitation. *IEEE Transactions on Neurological Systems and Rehabilitation Engineering*, 9, 308-318.

Jacobs, W.J., Laurance, H.E., & Thomas, K. (1997). Place learning in virtual space I: Acquisition, overshadowing and transfer. *Learning and Motivation.* 28, 521-541.

Jaffe, D. L., Brown, D. A., Pierson-Carey, C. D., Buckley, E. L., & Lew, H. L. (2004). Stepping over obstacles to improve walking in individuals with poststroke hemiplegia. *Journal of rehabilitation research and development*, *41*(3), 283.

Jentsch, F., & Curtis, M. (2017). Simulation in aviation training. Routledge.

Jin, W., Choo, A., Gromala, D., Shaw, C., & Squire, P. (2016). A Virtual Reality Game for Chronic Pain Management: A Randomized, Controlled Clinical Study. *Stud Health Technol Inform*, *220*, 154-60.

John, N. W., Pop, S. R., Day, T. W., Ritsos, P. D., & Headleand, C. J. (2017). The Implementation and Validation of a Virtual Environment for Training Powered Wheelchair Manoeuvres. *IEEE Transactions on Visualization and Computer Graphics*. http://dx.doi.org/10.1109/TVCG.2017.2700273

Johnston, R. (1995). Is it live or is it memorized? Virtual Reality Special Report. 2, 53-56.

Josman, N., Ben-Chaim, H. M., Friedrich, S., & Weiss, P. L. (2008). Effectiveness of virtual reality for teaching street-crossing skills to children and adolescents with autism. *International Journal on Disability and Human Development*, *7*(1), 49-56.

Josman, N., Kizony, R., Hof, E., Goldenberg, K., Weiss, P.L., & Klinger, E. (2014). Using the virtual action planning-supermarket for evaluating executive functions in people with stroke. *Journal of Stroke and Cerebrovascular Diseases, 23(5),* 879-887.

Kaplan, A.Y., Shishkin, S.L., Ganin, I.P., Basyul, I.A., & Zhigalov, A.Y. (2013). Adapting the P300-based brain-computer interface for gaming: a review. *IEEE Transactions on Computational Intelligence and AI in Games*. DOI: 10.1109/TCIAIG.2012.2237517.

Kato, P. M. (2010). Video games in health care: Closing the gap. *Review of General Psychology*, *14*(2), 113.

Keefe, R.S.E., Davis, V.G., Atkins, A.S., Vaughan, A., Patterson, T., Narasimhan, M., & Harvey, P.D. (2016). Validation of a Computerized Test of Functional Capacity. *Schizophrenia Research*, *175*(*1*-3), 90-96.

Klamroth-Marganska, V., Blanco, J., Campen, K., Curt, A., Dietz, V., Ettlin, T., Felder, M., Fellinghauer, B., Guidali, M., Kollmar, A., Luft, A., Nef, T., Schuster-Amft, C., Stahel, W., & Riener, R. (2014). Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomised trial. *The Lancet Neurology*, *13*(2): 159-166.

Klinger, E. (2005). *Virtual reality therapy for social phobia: Its efficacy through a control study*. Paper presented at Cybertherapy 2005 (July 7-10), Basal, Switzerland.

Kober, S.E., Wood, G., Hofer, D., Kreuzig, W., Kiefer, M., & Neuper, C. (2013). Virtual reality in neurologic rehabilitation of spatial disorientation. *Journal of NeuroEngineering and Rehabilitation.* doi:10.1186/1743-0003-10-17.

Koenig, S. T. (2012). *Individualized virtual reality rehabilitation after brain injuries*. (Unpublished doctoral dissertation). Human Interface Technology Lab New Zealand, College of Engineering, University of Canterbury, Christchurch, New Zealand.

Koenig, S.T., Crucian, G.P., Dalrymple-Alford, J.C., & Dünser, A. (2010). Assessing navigation in real and virtual environments: a validation study. *Proceedings of the International Conference Series on Disability, Virtual Reality and Associated Technologies (ICDVRAT)*, Vina del Mar, Chile.

Koenig, S.T., Krch, D., Chiaravalloti, N., Lengenfelder, J., Nikelshpur, O., Lange, B.S., DeLuca, J., & Rizzo, A.A. (2012). User-centered development of a virtual reality cognitive assessment. *Proc. 9th Intl Conf. Disability, Virtual Reality & Associated Technologies, Laval, France.*

Krch, D., Koenig, S., Lavrador, S., Rizzo, A., & Chiaravalloti, N. D. (2013, August 26-29). *Pilot results from a virtual reality executive function task.* Paper presented at the proceedings of the International Conference on Virtual Rehabilitation, Philadelphia, PA.

Krueger, M.W. (1993). The experience society. Presence, 2, 162-168.

Lamson, R.J. (1994). Virtual therapy of anxiety disorders. Cyberedge Journal, 4(1), 6-8.

Lange, B.S., Flynn, S.M., Proffitt, R., Chang, C.Y., & Rizzo, A.A. (2010). Development of an interactive game-based rehabilitation tool for dynamic balance training. Topics in Stroke Rehabilitation, 17(5), 345–352.

Lange, B.S., Flynn, S.M., & Rizzo, A.A. (2009). Initial usability assessment of off-the-shelf video game consoles for clinical game-based motor rehabilitation. Physical Therapy Reviews, 14(5), 355-363.

Lange, B., Koenig, S., Chang, C-Y., McConnell, E., Suma, E., Bolas M. & Rizzo, A.A. (2012). Designing Informed Game-Based Rehabilitation Tasks Leveraging Advances in Virtual Reality. *Disability and Rehabilitation*. 34(22): 1863-1870.

Lanyi, C.S., Brown, D.J., Standen, P., Lewis, J., & Butkute, V. (2012). Results of User Interface Evaluation of Serious Games for Students with Intellectual Disability. *Acta Polytechnica Hungarica*, *9*(*1*), 225-245.

Larson, E.B., Feigon, M., Gagliardo, P., & Dvorkin, A.Y. (2014). Virtual reality and cognitive rehabilitation: A review of current outcome research. *NeuroRehabilitation, 34*, 759-772. DOI:10.3233/NRE-141078.

LaViola, J. J., Jr., Kruijff, E., McMahan, R. P., Bowman, D., & Poupyrev, I. P. (2017). 3D user interfaces: Theory and practice (2nd ed.). Boston: Addison Wesley.

Levin, M., Weiss, P.L., & Keshner, E.A. (2015). Emergence of Virtual Reality as a Tool for Upper Limb Rehabilitation. *Physical Therapy*, *95*, 415-425.

Levy, C. E., Halan, S., Silverman, E. P., Marsiske, M., Lehman, L., Omura, D., & Lok, B. C. (2015). Virtual environments and virtual humans for military mild traumatic brain injury and posttraumatic stress disorder: an emerging concept. *American Journal of Physical Medicine & Rehabilitation*, *94*(4), e31-e32.

Liu, L., Miyazaki, M. & Watson, B. (1999). Norms and validity of the DriVR: A virtual reality driving assessment for persons with head injuries. *Cyberpsychology & Behavior, 2*, 53-67.

Lucas, G.M., Gratch, J., King, A., and Morency, L.-P. (2014). It's only a computer: Virtual humans increase willingness to disclose. *Computers in Human Behavior*, 37, 94–100.

Lumbreras, M. & Sanchez, J. (2000). Usability and cognitive impact of the interaction with 3D virtual interactive acoustic environments by blind children. In Sharkey, P., Cesarani, A., Pugnetti, L. & Rizzo, A. (Eds.), *Proceedings of the 3rd International Conference on Disability, Virtual Reality, and Associated Technology.* Reading, UK: University of Reading, 129-136.

Madary, M., & Metzinger, T. K. (2016). Real virtuality: a code of ethical conduct. recommendations for good scientific practice and the consumers of vr-technology. *Frontiers in Robotics and AI*, *3*, 3.

Man, D.W.K., Ganesan, B., Yip, C.C.K., Lee, C.O.P., Tsang, S.Y.L., Yu, P.W.P., et al. (2016). Validation of the virtual-reality prospective memory test (Hong Kong Chinese version) for individuals with first-episode schizophrenia. *Neuropsychological Rehabilitation*, http://dx.doi.org/10.1080/09602011.2016.1251949.

Maples-Keller, J. L., Bunnell, B. E., Kim, S. J., & Rothbaum, B. O. (2017). The Use of Virtual Reality Technology in the Treatment of Anxiety and Other Psychiatric Disorders. *Harvard review of psychiatry*, *25*(3), 103-113.

Matheis, R., Schultheis, M.T., Tiersky, L.A., DeLuca, J., Mills, S.R. and Rizzo, A.A. (2007). Is learning and memory different in a virtual environment? *The Clin Neuropsych.* 21, 146-161.

McCall, C., Blascovich, J., Young, A., & Persky, S. (2009). Proxemic behaviors as predictors of aggression towards Black (but not White) males in an immersive virtual environment. *Social Influence*, *4*(2), 138-154.

McComas, J., MacKay, M. & Pivak, J. (2002). Effectiveness of virtual reality for teaching pedestrian safety. *CyberPsychology and Behavior, 5,* 185-190.

McGeorge, P., Phillips, L.H., Crawford, J.R., Garden, S.E., Della Sala, S., Milne, A.B., Hamilton, S. & Callander, J. (2001). Using virtual environments in the assessment of executive dysfunction. *Presence-Teleoperators and Virtual Environments. 10*, 375-383.

Merians, A. S., Jack, D., Boian, R., Tremaine, M., Burdea, G. C., Adamovich, S. V., Poizner, H. (2002). Virtual reality–augmented rehabilitation for patients following stroke. Physical therapy, 82(9), 898-915.

Merians, A. S., Fluet, G. G., Qiu, Q., Saleh, S., Lafond, I., & Adamovich, S. V. (2010). Integrated arm and hand training using adaptive robotics and virtual reality simulations. In P. Sharkey & J. Sánchez (Eds.) *Proceedings of the 2010 International Conference on Disability, Virtual Reality and Associated Technology* (pp. 213-222). Reading UK: University of Reading.

Millan, J.d.R., Rupp, R., Müller-Putz, G.R., Murray-Smith, R., Giugliemma, C., et al. (2010). Combining brain-computer interfaces and assistive technologies: state-of-the-art and challenges. *Frontiers in Neuroscience*, https://doi.org/10.3389/fnins.2010.00161

MindMaze (2017). MindMaze MindMotion, Retrieved from https://www.mindmaze.com/mindmotion/

Moncur, M. & Moncur, L. (2002). QuotationsPage.com. At: http://www.quotationspage.com/quotes/Plato/

Morbini, F., DeVault, D., Sagae, K., Gerten, J., Nazarian, A., & Traum, D. (2014). FLoReS: A forward looking, reward seeking, dialogue manager. In J. Mariani, S. Rosset, M. Garnier-Rizet, L. Devillers (Eds.). *Natural interaction with robots, knowbots and smartphones* (pp. 313–325). New York, NY: Springer. http://dx.doi.org/10.1007/978-1-4614-8280-2_28

Morina, N., Ijntema, H., Meyerbr€oker, K., & Emmelkamp, P. M. G. (2015). Can virtual reality exposure therapy gains be generalized to real-life? A meta-analysis of studies applying behavioral assessments. *Behaviour Research and Therapy*, 74, 18e24.

Morrison, J.E. & Meliza, L.L. (1999). Foundations of the after action review process. U.S. Army Research Institute for the Behavioral and Social Sciences Special Report #42.

Morrongiello, B.A., Corbett, M., Switzer, J., & Hall, T. (2015). Using a Virtual Environment to Study Pedestrian Behaviors: How Does Time Pressure Affect Children's and Adults' Street Crossing Behaviors? *Journal of Pediatric Psychology*, *40*(7), 697-703.

Mosadeghi, S., Reid, M.W., Martinez, B., Rosen, B.T., & Spiegel, B.M.R. (2016). Feasibility of an Immersive Virtual Reality Intervention for Hospitalized Patients: An Observational Cohort Study. *JMIR Ment Health, 3(2)*, e28. doi: 10.2196/mental.5801. Mowafty L. & Pollack, J. (1995). Train to travel. *Ability, 15*, 18-20.

Mühlberger, A., Jekel, K., Probst, T., Schecklmann, M., Conzelmann, A., Andreatta, M., Rizzo, A.A., Pauli, P., & Romanos, M. (2016). The Influence of Methylphenidate on Hyperactivity and Attention Deficits in ADHD: A Virtual Classroom Test. *Journal of Attention Disorders*.

Navarro, MD.; Lloréns Rodríguez, R.; Noé, E.; Ferri, J.; Alcañiz Raya, ML. (2013). Validation of a low-cost virtual reality system for training street-crossing. A comparative study in healthy, neglected and non-neglected stroke individuals. Neuropsychological Rehabilitation. 23(4):597-618. doi:10.1080/09602011.2013.806269.

Naveh, Y., Katz, N. & Weiss, P. (2000). The effect of interactive virtual environment training on independent safe street crossing of right CVA patients with unilateral spatial neglect. In Sharkey, P., Cesarani, A., Pugnetti, L. & Rizzo, A. (Eds.), *Proceedings of the 3rd*

International Conference on Disability, Virtual Reality, and Associated Technology. Reading, UK: University of Reading, 243-248.

Neisser, U. (1978). Memory: what are the important questions? In M. M. Gruneberg, P. E. Morris, & R. N. Sykes (Eds.), *Practical Aspects of Memory*. London: Academic Press. 3-24.

Neri, S.G.R., Cardoso, J.R., Cruz, L., Lima, R.M., de Oliveira, R.J., Iversen, M.D., & Carregaro, R.L. (2017). Do virtual reality games improve mobility skills and balance measurements in community-dwelling older adults? Systematic review and meta-analysis. *Clinical Rehabilitation.* http://dx.doi.org/10.1177%2F0269215517694677

Nir-Hadad, S. Y., Weiss, P. L., Waizman, A., Schwartz, N., & Kizony, R. (2017). A virtual shopping task for the assessment of executive functions: Validity for people with stroke. *Neuropsychological rehabilitation*, *27*(5), 808-833.

Norcross, J.C., Pfund, R.A., & Prochaska, J.O. (2013). Psychotherapy in 2022. A Delphi poll on its future. Professional Psychology: Research & Practice. *44*(5): 363–70.

Norrholm, S. D., Jovanovic, T., Gerardi, M., Breazeale, K. G., Price, M., Davis, M., Duncan, E., Ressler, K.J., Bradley, B., Rizzo, A., & Tuerk, P. W. (2016). Baseline psychophysiological and cortisol reactivity as a predictor of PTSD treatment outcome in virtual reality exposure therapy. *Behaviour research and therapy*, *82*, 28-37.

NVIS Inc (2017). NVIS Products, Retrieved from http://www.nvisinc.com/product/standard.html

Ogourtsova, T., Souza Silva, W., Archambault, P. S., & Lamontagne, A. (2017). Virtual reality treatment and assessments for post-stroke unilateral spatial neglect: a systematic literature review. *Neuropsychological rehabilitation*, *27*(3), 409-454.

Opris, D., et al., (2012). Virtual reality exposure therapy in anxiety disorders: A quantitative meta-analysis. *Depression and Anxiety*, *29*(2): p. 85-93.

Padgett, L., Strickland, D., & Coles, C. (2006). Case study: Using a virtual reality computer game to teach fire safety skills to children diagnosed with Fetal Alcohol Syndrome (FAS), *Journal of Pediatric Psychology*, 31(1), 65-70.

Papastergiou, M. (2009). Exploring the potential of computer and video games for health and physical education: A literature review. *Computers & Education*, 53(3), 603-622.

Park, S., Scherer, S., Gratch, J., Carnevale, P., & Morency, L. P. (2013, September). Mutual behaviors during dyadic negotiation: Automatic prediction of respondent reactions. In T. Pun, C. Pelachaud, N. Sebe (Eds). *2013 Humaine Association Conference on Affective Computing and Intelligent Interaction (ACII),* (pp. 423-428). Los Alomitos, CA: IEEE.

Parsons, T.D. (2015). Virtual Reality for Enhanced Ecological Validity and Experimental Control in the Clinical, Affective and Social Neurosciences. *Front. Hum. Neurosci., 9(660)*, https://doi.org/10.3389/fnhum.2015.00660

Parsons, S. Bauminger, N., Cobb, S., Gal, E., Glover, T., Weiss, P.L. Zancanaro, M., Eden, S., Garib-Penna, S., Hawkins, T., Millen, L., & Rietdijk, W. (2012). Collaborative Technologies for supporting social conversation and collaboration in the classroom: overview and findings of the COSPATIAL project. 1st International Conference on Innovative Technologies for Autism Spectrum Disorders. ASD: Tools, Trends and Testimonials in Valencia, Spain. July 6-8, 2012.

Parsons, T. D., Carlew, A. R., Magtoto, J., & Stonecipher, K. (2017). The potential of function-led virtual environments for ecologically valid measures of executive function in experimental and clinical neuropsychology. *Neuropsychological rehabilitation*, *27*(5), 777-807.

Parsons, T. D. & Rizzo, A. A. (2008a). Affective Outcomes of Virtual Reality Exposure Therapy for Anxiety and Specific Phobias: A Meta-Analysis. *Journal of Behavior Therapy and Experimental Psychiatry*, 39, 250-261.

Parsons, T.D. & Rizzo, A.A. (2008b). Initial Validation of a Virtual Environment for Assessment of Memory Functioning: Virtual Reality Cognitive Performance Assessment Test. *Cyberpsychology and Behavior*, 11(1), 17-25. Parsons, T.D., Rizzo, A.A., Rogers, S. and York, P. (2009). Virtual reality in paediatric rehabilitation: A review. *Developmental Neurorehabilitation*, 12:4 224-238. Parsons, T.D., Rizzo, A.A., Rogers, S. and York, P. (2009). Virtual reality in paediatric rehabilitation: A review. *Developmental Neurorehabilitation*, 12:4 224-238.

Passig, D., Tzuriel, D., & Eshel-Kedmi, G. (2016). Improving children's cognitive modifiability by dynamic assessment in 3D Immersive Virtual Reality environments. *Computers & Education, 95,* 296-308.

Pertaub, D-P., Slater, M., & Barker, C. (2002). An Experiment on Public Speaking Anxiety in Response to Three Different Types of Virtual Audience. *Presence.* 11(1), 68-78.

Pietrzak, E., Pullman, S., & McGuire, A. (2014). Using Virtual Reality and Videogames for Traumatic Brain Injury Rehabilitation: A Structured Literature Review. *Games For Health Journal: Research, Development, and Clinical Applications, 3(4)*, 202-215.

Piron, L., Tonin, P., Atzori, A. M., Zanotti, E., Massaro, C., Trivello, E., & Dam, M. (2001). Virtual environment system for motor tele-rehabilitation. *Studies in health technology and informatics*, *85*, 355-361.

Powers, M. and Emmelkamp, P. M. G. (2008). Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *Journal of Anxiety Disorders*. 22, 561-569.

Proffitt, R., & Lange, B. (2015). Feasibility of a Customized, In-Home, Game-Based Stroke Exercise Program Using the Microsoft Kinect® Sensor. *Int J Telerehabil, 7(2),* 23–34.

Pugnetti, L., Mendozzi, L., Motta, A., Cattaneo, A., Barbieri, E., and Brancotti, S. (1995). Evaluation and retraining of adults' cognitive impairments: Which role for virtual reality technology? *Computers in Biology and Medicine*, *25*, 213-227.

Putrino, D. (2014). Telerehabilitation and emerging virtual reality approaches to stroke rehabilitation. *Current Opinion in Neurology*, *27(6)*, 631-636.

Regenbrecht, H., Hoermann, S., Ott, C., Müller, L., & Franz, E. (2014). Manipulating the Experience of Reality for Rehabilitation Applications. *Proceedings of the IEEE, 102(2)*, 170-184. DOI: 10.1109/JPROC.2013.2294178.

Remsik, A., Young, B., Vermilyea, R., Kiekoefer, L., Abrams, J., et al. (2016). A review of the progression and future implications of brain-computer interface therapies for restoration of distal upper extremity motor function after stroke. *Expert Review of Medical Devices*. http://dx.doi.org/10.1080/17434440.2016.1174572

Riva, G. (2011). The Key to Unlocking the Virtual Body: Virtual Reality in the Treatment of Obesity and Eating Disorders. *Journal of Diabetes Science and Technology*, 5(2), 283-292.

Rizzo, A.A. (1994). Virtual Reality applications for the cognitive rehabilitation of persons with traumatic head injuries. In Murphy, H.J. (ed.), Proceedings of the 2nd International Conference on Virtual Reality And Persons With Disabilities. CSUN: Northridge. (available at: http://www.csun.edu/cod/conf/1994/proceedings/Table94.htm)

Rizzo, A.A., Buckwalter, J.G., and Neumann, U. (1997). Virtual reality and cognitive Rehabilitation: A brief review of the future. *The Jour. of Head Trauma Rehab.*, *12*(6),1-15.

Rizzo, M., Reinach, S., McGehee, D., & Dawson, J. (1997). Simulated car crashes and crash predictors in drivers with Alzheimer disease. *Archives of neurology*, *54*(5), 545-551.

Rizzo, A.A., Buckwalter, J.G., Humphrey, L., van der Zaag, C., Bowerly, T., Chua, C., Neumann, U., Kyriakakis, C., van Rooyen, A. & Sisemore, D. (2000). The Virtual Classroom: A Virtual Environment for the Assessment and Rehabilitation Of Attention Deficits. *CyberPsychology and Behavior*, *3*(3), 483-499.

Rizzo, A., Schultheis, M. T., & Rothbaum, B. O. (2003). Ethical issues for the use of virtual reality in the psychological sciences. In S. S. Bush, & M. L. Drexler (Eds.), *Ethical issues in clinical neuropsychology*, (pp. 243–280), Amsterdam NL: Swets & Zeitlinger.

Rizzo, A.A., Schultheis, M.T., Kerns, K. and Mateer, C. (2004). Analysis of Assets for Virtual Reality Applications in Neuropsychology. *Neuropsychological Rehabilitation*, 14(1/2), 207-239.

Rizzo, A.A., Strickland, D. & Bouchard, S. (2004). Issues and Challenges for Using Virtual Environments in Telerehabilitation. *Telemedicine Journal and e-Health*, 10(2), 184-195.

Rizzo, A.A., Bowerly, T., Buckwater, J.G., Klimchuk, D., Mitura, R., & Parsons, R.D. (2006). A virtual reality scenario for all seasons: the virtual classroom. *CNS Spectums*, 11(1). 35-44.

Rizzo, A., Difede, J., Rothbaum, B.O., and Reger, G. (2010). Virtual Iraq/Afghanistan: Development and early evaluation of a Virtual Reality Exposure Therapy System for combatrelated PTSD. *Annals of the New York Academy of Sciences (NYAS*), 1208, 114-125.

Rizzo, A.A., Kenny, P. & Parsons, T., (2011). Intelligent Virtual Humans for Clinical Training. *International Journal of Virtual Reality and Broadcasting*, 8(3), Available: http://www.jvrb.org/8.2011/

Rizzo, A.A., Buckwalter, J.G., Forbell, E., Reist, C., Difede, J., Rothbaum, B.O., Lange, B., Koenig, S. & Talbot, B. (2013). Virtual Reality Applications to Address the Wounds of War. *Psychiatric Annals*, 43 (3), 123-138.

Rizzo, A.A., Cukor, J., Gerardi, M., Alley, S., Reist, C., Roy, M., Rothbaum, B.O., & Difede, J. (2015a). Virtual Reality Exposure Therapy for PTSD due to Military Combat and Terrorist Attacks. *Journal of Contemporary Psychotherapy*, 45(4), 255-264.

Rizzo, A.A., Shilling, R., Forbell, E., D., Scherer, S., Gratch, J., & Morency, L-P. (2015b). Autonomous Virtual Human Agents for Healthcare Information Support and Clinical Interviewing. In: Luxton, D.D. (Ed). *Artificial Intelligence in Mental Healthcare Practice*. Academic Press: Oxford. 53-80. Rizzo, A.A. & Talbot, T. (2016a). Virtual Reality Standardized Patients for Clinical Training. In: Combs, C.D., Sokolowski, J.A. & Banks, C.M. (Eds). *The Digital Patient: Advancing Medical Research, Education, and Practice.* Wiley: New York. 257-272.

Rizzo, A. A., Lucas, G., Gratch, J., Stratou, G., Morency, L.-P., Shilling, R., & Scherer, S. (2016b). Clinical interviewing by a virtual human agent with automatic behavior analysis. In P. Sharkey and A.A. Rizzo (Eds.) *2016 Proceedings of the International Conference on Disability, Virtual Reality and Associated Technologies,* (p. 57-64) Reading UK: University of Reading. Available at:

http://www.icdvrat.org/2014/papers/ICDVRAT2014_S03N3_Rizzo_etal.pdf

Robertson, I. (1990). Does computerized cognitive rehabilitation work? A review. *Aphasiology*, *4*(*4*), 381-405.

Rose, F.D., Attree. E.A., Brooks, B.M. & Andrews, T.K. (2001). Learning and memory in virtual environments - a role in neurorehabilitation? Questions (and occasional answers) from UEL. *Presence-Teleoperators and Virtual Environments. 10,* 345-358.

Rose, D., Brooks, B.M. & Attree, E.A. (2000). Virtual reality in vocational training of people with learning disabilities. In Sharkey, P., Cesarani, A., Pugnetti, L. & Rizzo, A. (Eds.), *Proceedings of the 3rd International Conference on Disability, Virtual Reality, and Associated Technology*. Reading, UK: University of Reading. 129-136.

Rose, F.D., Brooks, B.M. and Rizzo, A.A. (2005). Virtual Reality in Brain Damage Rehabilitation: Review. *CyberPsychology and Behavior*. 8(3), 241-262.

Rothbaum, B.O. & Hodges, L.F. (1999). The Use of Virtual Reality Exposure in the Treatment of Anxiety Disorders. *Behavior Modification*, *23(4)*, 507-525.

Rothbaum, B. O., Hodges, L. F., Kooper, R., Opdyke, D., Williford, J. S., & North, M. (1995). Virtual reality graded exposure in the treatment of acrophobia: A case report. *Behavior Therapy*, *26*(3), 547-554.

Rothbaum, B.O., Hodges, L., Ready, D., Graap, K. and Alarcon, R. (2001). Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. *Journal of Clinical Psychiatry*, *62*, 617-622.

Rothbaum, B.O., Price, M., Jovanovic, T., Norrholm, S., Gerardi, M., Dunlop, B., Davis, M., Bradley, B., Duncan, E.J., Rizzo, A., Ressler, K. (2014). A Randomized, Double-blind Evaluation of D-Cycloserine or Alprazolam Combined with Virtual Reality Exposure Therapy for Posttraumatic Stress Disorder (PTSD) in OEF/OIF War Veterans. *American Journal of Psychiatry*, *171*, 640-648.

Roy, M.J., Costanzo, M.E., Blair, J.R. & Rizzo, A.A. (2014). Compelling Evidence that Exposure Therapy for PTSD Normalizes Brain Function. *Studies in HealthTechnology and Informatics*, *199*, 61-65.

Roy, M.J., Francis, J., Friedlander, J., Banks-Williams, L., Lande, R.G., Taylor, P., Blair, J., McLellan, J., Law, W., Tarpley, V., & Patt, I. (2010). Improvement in cerebral function with treatment of posttraumatic stress disorder. *Annals of the New York Academy of Sciences*, *1208*(1), 142-149.

Rutten, A., Cobb, S., Neale, H., Kerr, S. Leonard, A., Parsons, S., & Mitchell, P. (2003). The AS interactive project: single-user and collaborative virtual environments for people with

high-functioning autistic spectrum disorders. *Journal of Visualization and Computer Animation.* 14(5), 233-241.

Sbordone, R. J., & Long, C. (1996). *Ecological validity of neuropsychological testing*. Boca Raton, FL: CRC Press.

Schell, J. (2014). *The art of game design: A book of lenses*. Boca Raton, FL: CRC Press. http://dx.doi.org/10.1201/b17723

Scherer, S., Stratou, G., Lucas, G., Mahmoud, M., Boberg, J., Gratch, J., Rizzo, A.A. & Morency, LP. (2014). Automatic Audiovisual Behavior Descriptors for Psychological Disorder Analysis. *Image and Vision Computing.* 32. 648–658.

Schneider, S.M., Kisby, C.K. and Flint, E.P. (2010, December 10, 2010). Effect of virtual reality on time perception in patients receiving chemotherapy. *Supportive Care in Cancer*, *19(4)*, 555-564. DOI: 10.1007/s00520-010-0852-7.

Schultheis M.T. & Mourant, R.R. (2001). Virtual Reality and Driving: The Road to Better Assessment of Cognitively Impaired Populations. *Presence: Teleoperators and Virtual Environments, 10,* 436-444.

Schwebel, D.C., McClure, L.A., & Severson, J. (2014). Teaching Children to Cross Streets Safely: A Randomized Controlled Trial, *Health Psychol, 33(7)*, 628–638. doi:10.1037/hea0000032.

Shipman, S., and Astur, R. (2008). Factors affecting the hippocampal BOLD response during spatial memory. *Behavioural Brain Research*. 187(2). 433-441.

SilverFit (2017). SilverFit Applications, Retrieved from http://silverfit.com/en/applications.

Skelton, RW, Bukach, CM, Laurance, HE, Thomas, KG, Jacobs, J. (2000). Humans with traumatic brain injuries show place learning deficits in computer generated virtual space. *J Clin Exp Neuropsychol.* 22; 157-175.

Slater, M. & Sanchez-Vives, M.V. (2016). Enhancing Our Lives with Immersive Virtual Reality. *Frontiers in Robotics and Artificial Intelligence*. Published: 19 December 2016. doi: 10.3389/frobt.2016.00074.

Sohlberg, M.K.M. & Mateer, C.A. (1989). *Introduction to cognitive rehabilitation: Theory and practice*. The Guilford Press, New York, NY, USA.

Sohlberg, M.K.M. & Mateer, C.A. (2001). *Cognitive Rehabilitation: An Integrative Neuropsychological Approach*. The Guilford Press, New York, NY, USA.

Spek, V., Cuijpers, P., Nyklicek, I., Riper, H., Keyzer, J., & Pop., V. (2007). Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychological Medicine*, *37*, 319-328.

Stamm, B. H. (1998). Clinical applications of telehealth in mental health care. *Professional Psychology: Research and Practice*, 29(6), 536.

Standen, P. J., Threapleton, K., Connell, L., Richardson, A., Brown, D. J., Battersby, S., ... Platts, F. (2014). Patients' use of home-based virtual reality system to provide rehabilitation of the upper limb following stroke. *Physical therapy*, *95*(3), 350-359. http://irep.ntu.ac.uk/id/eprint/25917/1/221608_PubSub3351_Brown.pdf Stanton, D., Foreman, N. and Wilson, P. (1998). Uses of virtual reality in clinical training: Developing the spatial skills of children with mobility impairments. In Riva, G., Wiederhold, B. and Molinari, E. (Eds.), *Virtual reality in clinical psychology and neuroscience*. Amsterdam: IOS Press. 219-232.

Strickland, D. (2001, August 16). *Virtual reality and multimedia applications for mental health assessment and treatment.* Paper presented at the ACM SIGGRAPH 2001 Conference. Los Angeles, CA. Aug. 12-17, 2001.

Talbot, T.B., Sagae, K., John, B., Rizzo, A.A. (2012). Sorting out the Virtual Patient: How to exploit artificial intelligence, game technology and sound educational practices to create engaging role-playing simulations. *International Journal of Gaming and Computer-Mediated Simulations*, *4*(3). 1-19.

Tarr, M. J., & Warren, W. H. (2002). Virtual reality in behavioral neuroscience and beyond. *Nature Neuroscience*, *5*, 1089-1092.

Tart, C. T. (1993). *Mind embodied: Computer generated virtual reality as a new, interactive dualism*. In K. Ramakrishna Rao (Ed.), Cultivating consciousness (pp. 123–137). Santa Barbara, CA: Praeger.

Tashjian, V.C., Mosadeghi, S., Howard, A.R., Lopez, M., Dupuy, T., et al. (2017). Virtual Reality for Management of Pain in Hospitalized Patients: Results of a Controlled Trial. *JMIR Ment Health, 4(1)*, e9. doi: 10.2196/mental.7387.

Tegos, S., Demetriadis, S., Papadopoulos, P. M., & Weinberger, A. (2016). Conversational agents for academically productive talk: a comparison of directed and undirected agent interventions. *International Journal of Computer-Supported Collaborative Learning*, *11*(4), 417-440.

Thiebaux, M., Marsella, S., Marshall, A. N., & Kallmann, M. (2008, May). Smartbody: Behavior realization for embodied conversational agents. In L. Padgham & D. Parkes (Eds.), *Proceedings of the 7th international joint conference on Autonomous agents and multiagent systems-Volume 1* (pp. 151-158). Estoril, Portugal — May 12-16, 2008. New York, NY: ACM.

Trost, Z., Zielke, M., Guck, A., Nowlin, L., Zakhidov, Z., France, C.R., & Keefe F. (2015). The promise and challenge of virtual gaming technologies for chronic pain: the case of graded exposure for low back pain. *Pain Management,* DOI: 10.2217/pmt.15.6.

Valladares-Rodriguez, S., Perez-Rodriguez, R., Anido-Rifon, L., & Fernandez-Iglesias, M. (2016). Trends on the application of serious games to neuropsychological evaluation: A scoping review. *Journal of Biomedical Informatics, 64*, 296-319. http://dx.doi.org/10.1016/j.jbi.2016.10.019

Valve Corporation (2017). Steam. Retrieved from http://store.steampowered.com/

Virtual Reality Society. (2017). Applications of Virtual Reality. Retrieved from: https://www.vrs.org.uk/virtual-reality-applications/

Wall, K.J., Cumming T.B., Koenig, S.T., Pelecanos, A.M., & Copland, D.A. (2017). Using technology to overcome the language barrier: The Cognitive Assessment for Aphasia App. *Disability and Rehabilitation.* http://dx.doi.org/10.1080/09638288.2017.1294210

Wiederhold, B.K. & Wiederhold, M.D. (1998). A review of virtual reality as a psychotherapeutic tool. *CyberPsychology and Behavior*, *1*, 45-52.

Wilson, B.A. (1997). Cognitive rehabilitation: How it is and how it might be. *Journal of the International Neuropsychological Society, 3.* 487 - 496.

Wilson, B.A., Baddeley, A. Evans, J., and Shiel, A. (1994). Errorless learning in the rehabilitation of memory impaired people. Neuropsychological Rehabilitation, 4(3), 307-326.

Wilson, B.A. & Evans, J.J. (1996). Error-free learning in the rehabilitation of people with memory impairments. *Journal of Head Trauma Rehabilitation, 11*, 54-64. Wilson, J, Onorati, K., Mishkind, M., Reger, M., & Gahm, G.A. (2008). Soldier attitudes about technology-based approaches to mental healthcare. *Cyberpsychol Behavior, 11*, 767–769.

Yang, Y. D., Allen, T., Abdullahi, S. M., Pelphrey, K. A., Volkmar, F. R., & Chapman, S. B. (2017). Brain responses to biological motion predict treatment outcome in young adults with autism receiving Virtual Reality Social Cognition Training: Preliminary findings. *Behaviour research and therapy*, *93*, 55-66.

Yellowlees, P.M., Holloway, K.M., & Parish, M.B. (2012). Therapy in Virtual Environments – Clinical and Ethical Issues. *Telemedicine and e-Health*, *18(7)*, 558-564. https://doi.org/10.1089/tmj.2011.0195.

You, S.H., Jang, S.H., Kim, Y.H., Hallett, M., Ahn, S.H., Kwon, Y.H., Kim, J.H. and Lee, M.Y. (2005). Virtual reality–induced cortical reorganization and associated locomotor recovery in chronic stroke. *Stroke*, *36*(6), 1166-1171.

Zhang, Z., Bickmore, T. W., & Paasche-Orlow, M. K. (2017). Perceived organizational affiliation and its effects on patient trust: Role modeling with embodied conversational agents. *Patient Education and Counseling*, 11, 417.