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COVER STORY:

Virtual Reality and Pharmaceuticals: Enhanced Synergy to Improve Clinical Care

and much more...
Via our combined communications platform, we inform and educate stakeholders on transforming healthcare through technology, leading the way to:

Patient Empowerment – Improved Dissemination of Services
Increased Quality of Life for all Citizens
Dear Reader,

In early 1996 we incorporated the use of real time non-invasive physiological monitoring into our clinical practice. For a busy therapist, patient preparation and application of sensors is relatively simple, and training is available for those who wish to learn to read the signals. For the therapist, the real-time information allows for individualization of therapy protocols, a means to compare progress over the course of multiple sessions, and quantitation of actual emotional reactions to specific cues and stressors. From a reimbursement point of view, the payors receive objective data where the physiology adds a more objective, quantitative component to validate success in the therapeutic intervention. In addition, it is possible to bring a more accurate prediction for the length of therapy and the associated costs. For patients, it helps them to more easily understand their stress and relaxation levels and results in transitioning of these skills into the real world setting. Empowering patients and providing them the opportunity to become more active participants in their own health and well-being builds self-efficacy and long-term sustainability of treatment results.

In order to overcome a fear or phobia, we must activate the fear structure and provide new information, that replaces pathological pathways and inefficient thoughts. Physiology shows both the patient and therapist objectively if the fear structure has been both accessed and activated. What is the role of cortisol in fear and its extinction?

Dr. Lang and colleagues first explained the neural foundations of fear. In our acrophobia scenario, when a person who is afraid of heights recognizes a potentially threatening or fearful situation, his/her brain responds to the stress by initiating a series of hormone secretions that eventually lead to stimulation of the fear structure.

Moving from measurement of cortisol levels to administration of cortisol, my colleagues and I, led by Dr. de Quervain, introduced 20 mg of oral cortisol given one hour prior to a virtual-elevator exposure therapy session. This resulted in a significantly greater reduction in the patient’s fear of heights in comparison to fear levels of patients given a placebo. Acrophobia questionnaires, a standard behavioral test used to assess fear of heights, and non-invasive physiology confirmed these results at post-treatment and at follow up one month after the treatment ended. Our results, which indicated that cortisol-enhanced exposure therapy more efficiently reduced acrophobia, are consistent with the idea that glucocorticoids facilitate fear extinction.

The cortisol in the bloodstream then causes an increase in blood glucose levels, which can be utilized by the brain and muscles to respond to the stressor.

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of the adrenal glands for cortisol secretion. The cortisol in the bloodstream then causes an increase in blood glucose levels, which can be utilized by the brain and muscles to respond to the stressor.

Researchers have begun using virtual reality scenarios with the Trier Social Stress Test (TSST) to activate the hypothalamic-pituitary-adrenal axis described above. A recent study used a TSST-adapted virtual environment in which a participant had to deliver a speech. The researchers found that 93% of the participants had increased cortisol levels, with this increase being statistically significant in the moment before the speech. Other researchers, using a TSST-adapted virtual reality CAVE™ system with three projected walls and one floor projection, found that while cortisol increased 88% above baseline when a participant was first tasked to give a speech, the rise in cortisol levels was not as dramatic in the second session. The authors concluded, “If these results can be replicated with larger samples, VR technology may be used as a simple and standardized tool for social stress induction in experimental settings.”

What are the next steps?

Additional studies combining VR and pharmacological agents are being conducted at the Virtual Reality Medical Center for the treatment of PTSD, the reduction of avoidance and fear in phobic subjects, and possible reduction of nightmares in PTSD. As the price of standard VR therapy continues to rapidly decline and the convenience of cloud-based applications grows, more widespread use is anticipated. More studies using fMRI and VR-compatible headsets are providing specific brain pathway activation in response to cues, stimuli and various cognitive tasks. These types of specific and well controlled studies bring a new level of precision to our understanding of how best to use these tools. Most importantly, identification of specific targets, whether they be receptors, neural pathways, or alterations in physiological response, will lead the way to newer and more effective interventions.

Create your own reality!

Brenda Wiederhold
CyberTherapy & Rehabilitation Magazine
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It’s All in Your Head

A sugar pill can regrow hair in a study on baldness; sham knee surgery can reduce pain comparable to real surgery. During World War II, a nurse injected a wounded soldier with salt water after heavy casualties depleted morphine supplies, giving the soldier enough pain relief to make it through surgery. The placebo effect describes this remarkable phenomenon that applying a treatment, any treatment, is likely to produce the desired results in medicine.

Enhancing VR Exposure Therapy Outcomes with Pharmaceutical Agents

The idea is to find out whether or not it is possible to enhance therapy outcomes by giving patients a pill during exposure therapy. This helps patients learn more easily how to overcome their anxiety during exposure therapy, making therapy more efficient in the long run. This idea is based on a learning paradigm wherein it is assumed that a learning process takes place during exposure.
Highlights of the
17th Annual CyberPsychology & CyberTherapy Conference

The 17th Annual CyberPsychology & CyberTherapy Conference: Experience the Future of Health & Well-Being (CYBER17), the official conference of the International Association of CyberPsychology, Training & Rehabilitation (iACTOR) was held September 25-28, 2012 in Brussels, Belgium. Prominent academic representatives from Europe, North America, and Asia served as Scientific Chairs and on its Scientific Committee. iACTOR’s Secretary General, Professor Brenda K. Wiederhold was the Conference Chair.

CYBER17 was truly an international success with 140 attendees from a multitude of disciplines and more than 20 countries. By locating the conference in Europe’s capital, CYBER17 provided a unique opportunity to raise the conference’s visibility and highlight the importance of technology and healthcare research. The presentations and discussions emphasized the need to enhance public awareness of how technology can overcome obstacles and increase access to top quality healthcare for all citizens.

CYBER17’s theme, Experience the Future of Health & Well-Being, explored the uses of advanced technologies through four main focus areas. First, the impact of technologies as tools being used in training, therapy, rehabilitation, and education for the improvement of the quality and availability of healthcare. Second, the influence of new technologies that furthers the investigation into how new technologies are influencing behaviour and society through the use of positive technology. Third, the imprint of social networking which explores its effects on individual behaviour and societal relations. Lastly, CYBER17 focused on the introduction of new technologies and terms on psychological aspects of areas influenced by technology such as cyberfashion, cyberadvertising, and cyberstalking.

Under the direction of Workshop Chair Stéphane Bouchard, CYBER17 kicked off with pre-conference workshops on Tuesday, the 25th of September. The workshops included a wide range of topics such as mobile technology for well-being, VR for mental health and brain computer interfaces.

The conference officially began on Wednesday, the 26th of September with a keynote address by Robert Madelin, Director-General of the European Commission’s Communications Network, Content & Technology Directorate (DG CONNECT) who spoke on “Cyberpsychology and Europe’s Digital Futures.” The second keynote speaker was Mary Baker, President of the European Brain Council, who gave a presentation on “Societal Challenges Facing Europe.”

“CYBER17 was truly an international success with attendees from more than 20 countries.”

The first symposium, Digital Societal Platforms, was chaired by Iliax Iakovidis and Peter Wintlev-Jensen, ICT for Digital Societal Platforms at the European Commission. This was followed by Health and Well-Being presentations which were chaired by Peteris Zilgalvis and Terje Peetsso from the ICT for Health and Wellbeing Unit. A PTSD symposia was chaired by Colonel Carl Castro of the U.S. Army Medical Research and Material Command.

Day 1 concluded with a poster session and Cyberarium. The poster session was an opportunity for developers and scientists to demonstrate their work and converse, one-on-one, with interested spectators and colleagues. The Cyberarium dedicated time for researchers to present their prototypes and for participants to experience their colleagues’ research, generating valuable feedback. After the scientific program, participants were invited to a welcome reception at Brussels Town Hall located in the historic Grand Place. Other conference highlights included a Gala Dinner that took place at Le Chalet Robinson and an awards ceremony.

Four students were presented with the Young Minds Research Award, Yoon Jung Choi, Haesol Hwang, Elisa Postrach and Maryan Ziekle. The 2012 Lifetime Achievement Award was given to Mariano Alcañiz for his outstanding work in the field. The New Investigator Award was given to Pietro Cipresso.

From the full day of pre-conference workshops to the groundbreaking scientific program, CYBER17 continued its role as the leading conference in designing the future of cyberpsychology and healthcare. It is with sincere appreciation and gratitude that we thank those who made this conference possible. CYBER17’s Scientific Committee Chairs, Professors Rosa Marie Baños, Willem-Paul Brinkman and Giuseppe Riva, were instrumental in providing exceptional scientific and social programs. The conference was also graciously sponsored by institutions and organizations whose important contributions allowed for a vibrant conference including Brussels Capital Region, the European Commission, DG CONNECT, Hanyang University, International Association of CyberPsychology, Training, & Rehabilitation (iACTOR), Interactive Media Institute (IMI), INTERSTRESS, ISfTeH, Istituto Auxologico Italiano, Mary Ann Liebert, Inc. Publishers, National Institute on Drug Abuse (NIDA), Université du Québec en Outaouais (UQO), the Virtual Reality Medical Center (VRMC), the Virtual Reality Medical Institute (VRMI) and Visit Brussels.
Highlights of the
17th Annual CyberPsychology & CyberTherapy Conference

Conference Chair B.K. Wiederhold, Keynote Speaker R. Madelin, & iACToR President G. Riva

Keynote Speaker Mary Baker, President European Brain Council

Mariano Alcaniz receiving the Lifetime Achievement Award

A happy audience at one of the many Symposiums

Students from Chung-Ang University enjoying the break

Conference members attending the poster session

Participants networking on a break at the EU Commission

Keynote address by Robert Madelin (DG-CONNECT)

VR demo at the Cyberarium
International Association of CyberPsychology, Training & Rehabilitation (iACToR)
Conference Participation Report 2012 / 2013

The Internet of Things Europe
Brussels, Belgium / www.internet-of-things.eu
November 12-13 2012,

The 4th Annual Internet of Things Europe explored the co-existence of real and virtual worlds in everyday life within areas such as health, transport and retail.

The Internet of Things Conference (IoT) in Brussels focused on the principle that connected devices and objects that are uniquely identifiable, are increasingly becoming reality, with related technologies rapidly finding their way into everyday life. In order to achieve a single market for IoT and maximize the advantages that a safe and advanced IoT would bring, policymakers, citizens and industry leaders together to collaborate.

The event facilitated debate among stakeholders on how both the public and private sectors need to work together to create an environment for increased innovation, investment and economic growth.

The EHTEL Symposium 2012
Brussels, Belgium / www.ehtel.org
December 6-7 2012,

Under the tag line “Fact not Fiction: The future of eHealth is already here”, the EHTEL Symposium 2012 held in Brussels, brought together leaders within the health, telematics and policymaking sectors.

Now that Telehealth is just as integrated in home care as telemedicine is in clinical routines, (e.g. for stroke) everyone in healthcare uses some digital communication. Yet while the tools are there, many conceptual, legal, organizational and educational challenges remain. Participants jointly learned and debated about citizen-centric concepts like the Coproduction of Health and the Digital Health Continuum. At the same time, the Symposium outlined the strategies and tactics that stakeholders can use to face today’s situation, and to do this in a way that is radically different from 2-3 years ago. The current fact is the old fiction.

The Medicine Meets Virtual Reality Conference
San Diego, California, USA / www.nextmed.com
February 21-23 2013,

INTERSTRESS members, Brenda K. Wiederhold (VRMI), Mark Wiederhold (VRMC) and Giuseppe Riva (Auxologico) chaired a half day symposium on Rehabilitation Tools / Psychology & Technology at the MMVR conference 2013. The INTERSTRESS results were discussed.

The 20th anniversary of the MMVR Conference held February of this year in San Diego attracted 288 people from around the world.

Three plenary sessions with featured speakers explored the forefront of health and medicine, while oral and poster presentations detailed critical developments in the field. Exhibits and demos provided tactile, one-on-one interaction, the Calit2 tour inspired visitors, and evening activities merged networking and fun.

The next conference MMVR21 will be held at Manhattan Beach, Los Angeles, California on February 20 - 22, 2014. Mark your calendar!!

The mHealth Stakeholder Conference
Brussels, Belgium / www.moving-life.eu
April 18 2013,

Mobile Health (or mHealth) is a term that refers to the provision of medical services through the use of portable devices with the capability to create, store, retrieve, and transmit data via mobile communications.

European project Movinglife presented and discussed the mHealth roadmap offering stakeholders an opportunity to voice their perspectives and opinions on the future deployment and widespread use of mHealth.

The roadmaps addressed a broad group of fundamental issues such as: technology options for applications and services, options for new and improved medical guidelines; user empowerment, acceptance; ethics and privacy; socio-economic environments and policy and regulatory frameworks. The combined roadmaps will address a range of fundamental issues that are related to the vision of massive deployment and use of mHealth solutions to support lifestyle changes among citizens and improve disease management.
The quarterly CyberTherapy & Rehabilitation Magazine (C&R) covers clinically-focused and practice-driven articles, congress reports, news and other relevant topics appealing to a wider readership including industry professionals, policy makers, clinicians, and individual citizens.

Please visit www.vrphobia.eu for more information.

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The combined use of virtual reality (VR) and medication is an emerging technique that has been gaining public notice. Clinical psychologists and neuroscientists have been studying this approach for the treatment and/or management of various types of medical conditions. These include chronic pain management, anxiety relief, and trauma recovery. Some studies have also shown the usefulness of VR as a tool for information dissemination and for the testing of new pharmaceutical products. Several pharmaceutical companies have used VR to educate individuals about a mental health disorder, patient’s perspective and state of mind. These companies then taught participants how medication may help with alleviating symptoms.

**Pain Management**

In a study by Schmitt et al. (2011) on using virtual reality exposure therapy (VRET) for analgesia/pain reduction in pediatric patients who have to undergo physical therapy for burn injuries, they found that the patients responded positively to VRET for pain reduction. The patients with VRET during physical therapy had reported significantly reduced pain sensation than the control group (patients who were not given VRET during physical therapy). Furthermore, both groups showed equivalent or comparable increase in range of motion, regardless of whether they were treated with VRET or not. Thus, this shows that VRET can be used in conjunction with physical therapy to relieve pain without any detriment to the patients’ physical recovery. Another interesting point in this study is that the level of analgesia experienced by patients during physical therapy with VRET did not diminish over time. Instead, the pain relief provided by VRET remained constant throughout the entire duration of the study.

**Anxiety Relief**

VRET has been used to manage anxiety disorders over the last two decades by providing visual, auditory and kinesthetic stimulation. VRET places patients in a computer-generated world where they “experience” the various stimuli related to their fear or phobia. Its effectiveness in the treatment of multiple anxiety disorders has been established in controlled studies which have been replicated by researchers worldwide. The benefits of pharmaceutical drugs such as selective serotonin re-uptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), beta-blockers, and other anxiolytic medications for the treatment of anxiety disorders have long been established. However, many recent studies have shown the increased effectiveness of combining medication therapy with cognitive behavioral therapy (including VRET) to teach the patient an alternative way of managing his or her
Symptoms while medication is reduced (or completely discontinued). Using VRET is ideal for testing the effectiveness of the medication since it allows systematic stimuli to be administered to the patient in a controlled clinical setting.

**Specific Phobias**

In a study published in March 2011 in the Proceedings of the National Academy of Sciences (PNAS), de Quervain et al. reported on combined VRET and hormonal therapy (cortisol) in treating acrophobia (fear of heights). The results indicated that cortisol enhanced the effects of the VRET. Patients who received cortisol together with VRET showed significantly greater reduction in anxiety and fear compared to patients who received placebo. The overall anxiety and fear reduction was seen both right after the treatment (post-treatment) and at a follow-up assessment done after one month of the procedure being conducted.

Patients undertaking treatment due to a fear of driving or PTSD due to a motor vehicle accident have responded positively to VRET treatments while on medication therapy. If patients become nauseous within 90 to 120 seconds after the commencement of VR treatment, they are referred to a vestibular specialist to determine if there is a vestibular abnormality. In many instances, patients who feel nauseous 90 to 120 seconds after VR therapy start do have vestibular abnormalities. Patients who choose to continue with the VR therapy sessions, they can opt to take anti-nausea drugs such as dimenhydrinate (Dramamine) or ondansetron (Zofran) prior to VR therapy without diminishing the therapeutic benefits obtained from the treatment.

Other studies have also documented the use of beta-blockers and anxiolytic drugs in conjunction with VRET as effective treatments/therapies for glossophobia (fear of public speaking), aerophobia (fear of flying), and claustrophobia (fear of closed or narrow spaces).

**Posttraumatic Stress Disorder (PTSD)**

Apart from enhancing the effects of certain medications, the combined use of VR and pharmaceutical drugs has been utilized for the treatment of PTSD and so far has shown no negative effects in the general well-being of the patients. Veterans of the Iraq and Afghanistan wars (suffering from both PTSD and chronic pain) who were undergoing VRET treatment while on medication did not manifest any adverse reactions after the use of VRET.

In one study, VRET was utilized to reduce the retrieval of aversive memories in PTSD. By administering adrenaline along with glucocorticoids, which enhance the formation of new memories for emotionally arousing events, researchers were able to impair the memory retrieval processes. This seems to be effective in the reduction of excessive re-experiencing or reliving of traumatic memories.

“Apart from enhancing the effects of certain medications, the combined use of VR and pharmaceutical drugs has been utilized for the treatment of PTSD and so far has shown no negative effects in the general well-being of the patients.”

In another Virtual Reality Medical Center (VRMC) study conducted at Balboa Naval Hospital and Camp Pendleton (both in CA, USA), the VRET for PTSD symptoms proved successful in 80% of participants. Many of the individuals treated with VRET required medication in addition to therapy, but the medication did not diminish their ability to fully engage in and receive therapeutic benefits from VRET.

**Eating Disorders and Obesity**

In a preliminary study conducted by Riva et al. (2001), the researchers assessed the feasibility of using VR for the treatment of body image issues of obese patients and found that patients who were treated using VR showed better body satisfaction and motivation for change than patients who were treated with the cognitive-behavior approach. While this study spanned only a short period of time, the promising results can be explored further to improve and develop VR treatments for the psychological and mental state of obese patients who are trying to become more fit and lose weight.

The FDA has recently approved several new drugs to combat obesity and eating disorders. Many studies have shown that weight loss medication when combined with cognitive behavioral therapy-based interventions dramatically improves adherence and success. Virtual environments offer an enhanced venue for the delivery for CBT-based protocols and may prove extremely useful when combined with these new pharmacological agents.

**Test bed for New Medications and Medical Technologies**

VR can also be used to test the effects of certain medications prior to release. This nascent field is on the rise for increasing the efficacy of combined treatment. Using VR, the precise stimulus is isolated. It is relatively simple to add physiological monitoring and analyze the patient’s objective response as well as asking for their subjective ratings. This technique is a perfect test bed for observing patients’ emotional and physical state. With the addition of fMRI technology, we can see the precise effect medication is having on an individual while navigating a stressful, relaxing, or rehabilitating environment, which will help to better tailor drug delivery and allow for more individualized care.
Cognitive Effects of Medications Already on the Market

Another use of VR is to test the possible side effects of medications which have already been released on the market. While manufacturers and physicians generally advise patients to avoid certain activities (e.g., driving) while taking specific medications, the actual side effects of these medications have not been tested on humans. VR allows testing of these drugs’ effects in a safe and controlled clinical setting.

In recent years, there has been a heightened interest among researchers and clinicians in using VR technology to address additional driving-related issues. One study led by R. Mager evaluated a driving simulator using a motorway test-track to investigate the impact of a single oral dose of the SSRI sertraline on various cognitive functions related to driving tasks and objective driving performance. Results showed no evidence of drug-induced impairment of drivability in the simulator.

Another study examined 37 adults with Type 1 diabetes and their ability to drive in VR. Researchers manipulated participants’ blood glucose levels by giving them an intravenous insulin solution containing various amounts of sugar. At all three ranges of hypoglycemia, driving performance was found to be significantly impaired. Participants were more likely to swerve, brake inappropriately, and speed up in comparison to when their glucose levels were within normal limits. Even more surprising, less than 1/4 of the participants realized that their driving was impaired, while only 1/3 took corrective action by drinking soda or stopping driving, and most did not do so until their glucose levels were below 50 mg/dL. Non-invasive sensors were used to measure the patients’ blood glucose levels accurately during the task. By providing precise stimuli and measuring the participants’ reactions, more definitive results of the effect of medications were ascertained.

In another study, researchers at VRMC in San Diego enlisted 24 participants to compare the effects of three antihistamines: fexofenadine, loratadine, and cetirizine. At the beginning of each session, participants were given either one of the antihistamines or a sugar pill (placebo) to drink. After one hour (the time needed for the medications to take effect), the participants carried out a VR test of tracking ability while their heart rates and breathing patterns were monitored. They were then asked to fill out questionnaires rating their moods and sleepiness. After data gathering and analysis, the results showed that loratadine and/or fexofenadine affect drivers’ moods and cognition less than cetirizine, making loratadine or fexofenadine better choices for drivers who need to take antihistamines.

Educating and Providing Insights on Patient Conditions

“While manufacturers and physicians generally advise patients to avoid certain activities (e.g., driving) while taking specific medications, the actual side effects of these medications have not been tested on humans. VR allows testing of these drugs’ effects in a safe and controlled clinical setting.”

Virtual reality has so far shown a lot of promise in providing and/or supplementing medical treatment for patients. Not only that, it also helps physicians understand their patients by simulating a home with foot and hand controls which are designed to mimic and/or induce the fatigue felt by patients undergoing chemotherapy. Of course, this event was also used by the sponsoring pharmaceutical company to inform physicians that medications are available for chemotherapy-related anemia. Aside from that, this VR simulation did seem to help in educating physicians because 60% of them, after experiencing ICRA, said that it changed the way they would view and treat patients suffering from side effects of ongoing chemotherapy.

Virtual reality is a very promising tool that can help in the treatment, maintenance, and improvement of healthcare.

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The INTERSTRESS project aims to design, develop and test an advanced ICT-based solution for the assessment and treatment of psychological stress.

Objectives:

- Quantitative and objective assessment of symptoms using biosensors and behavioral analysis
- Decision support for treatment planning through data fusion and detection algorithms
- Provision of warnings and motivating feedback to improve compliance and long-term outcome

To reach these goals, INTERSTRESS will use a new e-Health concept: Interreality. What is Interreality? It is the integration of assessment and treatment within a hybrid, closed-loop empowering experience, bridging physical and virtual worlds into one seamless reality.

- Behavior in the physical world will influence the virtual world experience
- Behavior in the virtual world will influence the real world experience

These goals will be achieved through:

- 3D Shared Virtual World role-playing experiences in which users interact with one another
  - Immersive in the healthcare centre
  - Non-immersive in the home setting
- Bio and Activity Sensors (from the Real to the Virtual World)
  - Tracking of emotional/health/activity status of the user and influencing the individual’s experience in the virtual world (aspect, activity, and access)
- Mobile Internet Appliances (from the Virtual to the Real world)
  - Social and individual user activity in the virtual world has a direct link with user’s life through a mobile phone/PDA

Clinical use of Interreality is based on a closed-loop concept that involves the use of technology for assessing, adjusting and/or modulating the emotional regulation of the patient, his/her coping skills and appraisal of the environment based upon a comparison of the individual patient’s behavioural and physiological responses with a training or performance criterion. The project will provide a proof of concept of the proposed system with clinical validation.
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iACToR is the official voice and resource for the international community using advanced technologies in therapy, training, education, prevention, and rehabilitation.

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Our mission is to bring together top researchers, policy makers, funders, decision makers and clinicians, pooling collective knowledge to improve the quality, affordability, and availability of existing healthcare.

Ultimately, through international collaboration with the most eminent experts in the field, we are working to overcome obstacles and increase access to top-quality healthcare for all citizens. By enhancing public awareness of the possibilities that technology offers, we move toward changing and improving healthcare as it currently exists.

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A sugar pill can regrow hair in a study on baldness; sham knee surgery can reduce pain comparably to real surgery. During World War II, a nurse injected a wounded soldier with salt water after heavy casualties depleted morphine supplies, giving the soldier enough pain relief to make it through surgery. The placebo effect describes this remarkable phenomenon that applying a treatment, any treatment, is likely to produce the desired results … the placebo effect …”

By Ariana Anderson

To test whether a given medication is superior to merely giving out optimism, disguised as a sugar pill, during drug trials patients often must either be divided into two treatment groups, or tested twice, once on active medicine and once when given placebo medications. Although the placebo effect has known psychological correlates that make some people react more strongly than others, measuring the placebo effect without actually applying a placebo treatment has not previously been possible.

Recognizing this, Ariana Anderson and Mark Cohen from UCLA at the Laboratory of Integrative Neuroscience in the department of Psychiatry have developed a method of isolating and measuring the placebo effect in the brain using functional MRI. If the placebo has a consistent footprint its change can be measured during a trial. More significant “placebo” activations in the brain correspond to higher levels of the placebo effect within a patient. This means that the placebo effect can be quantified indirectly in people receiving a treatment, opening the possibility that drug trials may be run with only half the patients currently needed. With per-drug bench-to-bedside costs measured in the hundreds of millions of dollars, the savings could be dramatic. “Orphan drugs” are those developed for
D-Cycloserine Augmentation of Cognitive-Behavioral Therapy for Anxiety Disorders

“In Studies using IVET protocols, DCS has demonstrated efficacy for social anxiety disorder, but has yielded mixed results for obsessive compulsive disorder, panic disorder with agoraphobia, and posttraumatic stress disorder.”

By Cristian Sirbu et al.

Characterization of D-Cycloserine DCS was approved by the Food and Drug Administration in 1965 as a broad spectrum oral antibiotic for tuberculosis. Standard doses range from 250-500 mg and some patients...
can reach doses of 1g per day. Adverse side effects have been documented with doses of 1g per day and include headache, psychosis, seizures, or somnolence. The main contraindications are alcohol use, renal failure, epilepsy (increased risk of seizures), or pregnancy. In addition to its use as an antidepressant agent, DCS has been evaluated as a medication for schizophrenia and Alzheimer’s dementia, but with low efficacy. Pharmacokinetic studies of DCS indicate that after a single oral dose of 50 mg, the peak plasma level measured 1-2 hours after administration is 3.7 + 1.2 mg/dL, with an estimated 2.9 + 0.96 mg/dL peak cerebrospinal fluid level (80% of the peak plasma level).

Efficacy of D-Cycloserine augmentation of exposure therapy for anxiety disorders
In studies of exposure therapy augmentation, DCS is used at low isolated doses of 50-500mg either before or shortly after the exposure therapy session. In most studies, DCS is used in association with in vivo exposure therapy (IVET); however, few studies have explored the use of virtual reality exposure therapy (VRET) (see below). Virtual Reality Exposure Therapy (VRET) has documented efficacy in the treatment of specific phobias (acrophobia, flying phobia, claustrophobia, driving phobia, arachnophobia), panic disorder with agoraphobia, social anxiety disorder, and posttraumatic stress disorder.

The mechanisms of exposure therapy in IV and VRET involve activation of different physiological systems. Thus, IVET produces changes in heart rate and skin conductance (involving both behavioral activation and inhibition systems) while VRET produces changes in skin conductance (involving only the behavioral inhibition system); therefore, an important question is what effect does DCS have on IVET versus VRET? In studies to date, DCS was used exclusively as an enhancer of either IVET or VRET. In studies using IVET protocols, DCS has demonstrated efficacy for social anxiety disorder, but has yielded mixed results for obsessive-compulsive disorder, panic disorder with agoraphobia, and posttraumatic stress disorder.

Surprisingly, the number of studies investigating the association of DCS and VRET are limited. In two published studies, DCS was used in association with VRET for acrophobia. Ressler et al., administered 50 mg DCS, 500 mg DCS, or placebo two to four hours before two sessions of 30-minute VRET, and demonstrated higher reduction in acrophobic symptoms at one week and three months post treatment for DCS conditions compared with placebo. No difference was noted between 50 and 500 mg DCS. In a recent study in acrophobics, Tart et al. used a similar protocol; however, 50 mg DCS was administered immediately after the two 30-minute sessions of VRET. No difference was noted between the DCS and placebo groups; however, a reanalysis of the data indicated that DCS was superior to placebo only for patients who experienced a successful exposure session.

Contributions from our group
In the past few years, our research on DCS has been focused on two main areas: (1) physicochemical characterization of DCS for anxiety disorders, and (2) investigation of DCS efficacy in acrophobia and dental phobia.

1) Physicochemical characterization of DCS for anxiety disorders
We conducted extensive studies regarding stability and characterization of DCS reformulation. Most studies using DCS for anxiety disorders use 50 mg DCS capsules. Those are reformulated from the 250 mg Seromycin® capsules. Questions regarding stability as well as potential conversion of D-Cycloserine into L-Cycloserine are important when DCS is reformulated. Research in our lab has demonstrated good stability as well as a lack of conversion to L-Cycloserine during the reformulation of the 250 mg DCS capsules to 50 mg strength. Further, we have demonstrated that the DCS undergoes significant degradation at acidic pH. This brings an important question about the amount of DCS reaching the brain, especially at the low doses (50 mg) used in the treatment of anxiety disorders, considering degradation at the acidic pH in the stomach. This issue has stimulated our interest in identifying new delivery methods (transdermal and nasal) for DCS.

2) DCS efficacy in acrophobia and dental phobia.
In one of our current studies, we are comparing the efficacy of 50 mg DCS to placebo in acrophobics. The drugs are administered 30 minutes before a three-hour, one-session treatment with either IVET or VRET. This design will allow the first comparison of the effect of DCS on IVET versus VRET using self-report, clinical interview, a Behavioral Avoidance Task, and physiological outcomes (heart rate variability and skin conductance). To date, no side effects have been noted in our participants (either placebo or DCS); data collection is ongoing and no comparison is possible yet since the trial is double blinded.
In a second study, we are investigating the efficacy of 50 mg DCS for reducing anxiety during dental visits and dental avoidance in patients with dental phobia. DCS is administered immediately prior to two dental visits. This ongoing study will provide the first demonstration of DCS efficacy in the context of a naturalistic exposure conducted in the dental office by dental professionals (hygienists). Additionally, DNA and RNA analysis of blood cells collected at baseline, after each treatment session, and at one week follow-up will allow investigation of the moderating effects of genetic polymorphism on DCS efficacy, as well as gene expression profiles, associated with this treatment.

“DCS augmentation represents a significant avenue for optimizing the existing exposure therapy protocols for anxiety disorders, reducing the duration as well as the number of sessions.”

DCS are important and delineation of clinical parameters of DCS use in both IVER and VRET are critical steps in understanding the optimal use of this promising pharmacological agent.
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Can you Enhance Virtual Reality Exposure Therapy Outcome by adding Pharmaceutical Agents?

“a patient receives a pill during exposure therapy sessions to stimulate their brains, making successful confrontation with their possible fears.”

Imagine a therapy that is always successful and would hardly take any time. Instead of going to therapy once a week for months, your treatment would be completed in several weeks and you would be yourself, without your limiting fears. Recent research suggests an approach to more successful therapy outcomes. The idea is to find out whether or not it is possible to enhance therapy outcomes by giving patients a pill during exposure therapy, thus helping patients overcome anxiety during treatment. In turn this makes therapy more efficient in the long run. This idea is based on a learning paradigm wherein it is assumed that a learning process takes place during exposure.

This paradigm concerns the enhancement of emotional learning by administering a cognitive enhancer as adjunct to (virtual reality) exposure therapy. This means that a patient receives a pill during exposure therapy sessions to stimulate their brains, making successful confrontation with their fears possible. The idea is to augment the emotional learning process during therapy by stimulating the noradrenergic system, which is involved in the process of emotional learning. One such cognitive enhancer is Yohimbine hydrochloride (YOH). While a number of experimental lab studies find positive effects of cognitive enhancers, results of intervention research with patients suffering from anxiety disorders have been less consistent. In a randomized controlled trial, Powers et al (2009) had claustrophobic participants undergoing exposure in vivo in combination with YOH or a non-active placebo. The YOH group showed significantly better results on anxiety improvement than the placebo group. This indicated that administering a pill during exposure therapy might indeed improve the therapy outcome. A more
recent study consisted of participants with a fear of flying. They were treated with virtual reality exposure therapy and no additional benefits of YOH were demonstrated. Patients received four sessions of virtual reality exposure therapy for fear of flying, consisting of two virtual flights in each exposure session. Compared with patients who received the same therapy but a non-active placebo pill, patients who received YOH did not show better therapy outcomes. This was contrary to the expectation as the dosage was almost the same from another study. One possible alternative explanation would be that the effects of a cognitive enhancer as YOH are so small that the powerful instrument of exposure has overruled them.

Results of research into cognitive enhancers have yielded diverse results. Generally we can say that the success of such pharmacological agents is based on the interaction with the mechanism of the psychological intervention (Vervliet, 2008). But as suggested by Powers et al (2009), the attribution of an additional medication to exposure therapy can play a crucial role. Therefore it is important to take into account the attribution of the patients themselves.

To sum up, there has been extensive research into the learning paradigm with cognitive enhancers which has been used with non-anxious participants. In clinical research this does not provide us with sufficient information about the disorder and its treatment possibilities. One important instrument for translating this research in the future is virtual reality exposure therapy. It can provide an excellent research environment to further investigate treatment mechanisms and theoretical paradigms. Extensive and detailed standardization within this treatment can provide us with valuable information about therapeutical processes and its implications in clinical populations.

"One important instrument for translating this research in the future is virtual reality exposure therapy."

Figure 2: Patient undergoing Exposure Therapy monitored in the research environment.
Since its inception in 1997, the Virtual Reality Analgesia Program at the University of Washington (Seattle, WA) has sought to explore and understand the mechanisms, efficacy, safety and cost-effectiveness of virtual reality (VR) applications to the vexing and unsolved problem of clinical pain. This commitment to exploring nonpharmacologic approaches to pain management is important because pharmacologic pain medications (e.g., opioids/narcotics) alone often fail to control the intense acute pain patients experience after injury, after surgery, or during medical procedures. Furthermore, such analgesic medications all produce dose-related side effects that limit the quantity of drug that can safely be administered – the result often being incomplete pain relief and other discomfort (e.g., nausea). Lastly, repeated episodes of excessive pain and the regular use of large doses of opioid analgesics can have serious long-term consequences, including increased risk of chronic pain and opioid dependence.

Our program focuses on VR analgesia applications in clinical pain settings such as medical procedure-associated pain (e.g., wound care and rehabilitative physical therapy in patients with cutaneous burn injuries [Figure 1]), with a complementary laboratory research component whose two goals are to better understand the analgesic mechanisms of VR applications and to optimize their clinical use. Funding support for the program includes awards from the US National Institutes of Health, the Paul G. Allen Family Foundation, the International Anesthesia Research Foundation, the Scan-Design Inger/Jens Brun Foundation, and the Gustavus/Louise Pfeiffer Research Foundation.

The most carefully studied analgesic approach to date is “VR distraction” – an approach based on the premise that by immersing patients in an attention-grabbing, computer-generated, interactive virtual world that blocks the sights and sounds of the immediate medical care environment, their attention is pulled away from the concurrent painful stimulus of their injury or a therapeutic medical procedure, resulting in significantly reduced pain experience.”
ise that the human pain experience requires conscious attention toward a painful stimulus (nociception). By immersing patients in an attention-grabbing, computer-generated, interactive virtual world that blocks the sights and sounds of the immediate medical care environment, their attention is pulled away from the concurrent painful stimulus of their injury or a therapeutic medical procedure, resulting in significantly reduced pain experience. Our group created an interactive virtual environment specifically for this purpose (SnowWorld® [Figure 2]), and published the first report of VR distraction analgesia in Pain in 2000. Subsequently we have reported clinical success with VR distraction analgesia in various clinical pain settings including patients with cutaneous burn injuries, dental pain, urologic surgery, and post-operative rehabilitation. Since 2007, our investigations have resulted in 38 peer-reviewed publications in scientific journals, six textbook chapters and review articles, and one book, as well as collaborations for both clinical and research applications in civilian and military patient populations in ten centers in the US, Europe and the Middle East. Recently we have reported the first successful use of VR technology to facilitate hypnotic analgesia—inducing a hypnotic state and delivering hypnotic suggestions for reduced pain, improved function, and improved sleep—in patients with ongoing clinical pain following traumatic injuries.

Complementary laboratory studies allow VR analgesia techniques to be studied in a controlled setting in healthy volunteers exposed to carefully regulated experimental pain. To better understand the neurobiology of pain and analgesia, we employ technically advanced outcome-assessment tools—for example, functional MRI imaging of pain-related brain activity and connectivity—and novel combinations of therapies (e.g., VR distraction combined with pharmacologic opioid receptor blockade) that are often not possible to study in the clinical setting. These investigations fill gaps in our knowledge of how new VR analgesic techniques work, and enable their exploration and refinement before they are introduced to actual clinical care. As a result of such laboratory studies, we have demonstrated that VR distraction produces similar reductions in both subjective pain reports and pain-related brain activity as intravenous opioid analgesics.

“VR distraction produces similar reductions in both subjective pain reports and pain-related brain activity as intravenous opioid analgesics.”

(“we have reported clinical success with VR distraction analgesia in patients with cutaneous burn injuries, dental pain, urologic surgery, and post-operative rehabilitation.”)

Current efforts are exploring the relative roles of various central pain pathways and neurotransmitter systems, as well as the effect of user age (e.g., adolescent compared to older adults) on VR distraction analgesia.

Figure 2:
Screenshot image of the user’s view of SnowWorld® during immersive virtual reality distraction. Virtual world designed/developed by Hunter Hoffman and David Patterson, with software created by Firsthand Technologies. (copyright Hunter Hoffman, University of Washington)

These studies have also helped identify the VR hardware and software components most essential to the user’s sense of presence in the virtual world, and hence the analgesic success of VR distraction.
Wounds of War
A Subseries of the
NATO Science for Peace and Security Series - E:
Human and Societal Dynamics

Latest volumes:

Pain Syndromes – From Recruitment to Returning Troops
Wounds of War IV
Vol. 91: NATO Science for Peace and Security Series - E: Human and Societal Dynamics
Editor: B.K. Wiederhold
July 2012, 252 pp., hardcover
ISBN: 978-1-60750-985-1
Price: €120 / US$174

It has been shown that those who have served in both combat missions and peacekeeping operations are at increased risk for pain syndromes. Research suggests that this may result from their “wounds of war.” Some wounds may be “invisible,” such as depression, stress, and chronic pain, while others, such as physical disabilities, are more obvious. In October 2011, twenty-seven scientists and representatives from NATO and partner countries met in Südtirol, Austria for a three-day NATO Advanced Research Workshop entitled “Wounds of War: Pain Syndromes – From Recruitment to Returning Troops.”

The aim of this publication, which presents papers from that workshop, is to critically assess the existing knowledge and to identify directions for future actions. The book addresses four key questions:
1. Vulnerability to Pain Syndromes: Are certain types of people at a higher risk for pain syndromes (background, ethnicity, childhood trauma, etc.)?
2. Diagnosis and Assessment Issues of Pain Syndromes: Which methods are used to diagnose and assess pain?
3. Treatment of Pain Syndromes: What are the latest treatment and therapy opportunities for soldiers who experience pain syndromes?
4. Clinical Updates on Pain Syndromes: What can we learn from recent clinical updates on pain syndromes?

Coping with Blast-Related Traumatic Brain Injury in Returning Troops
Wounds of War III
Vol. 85: NATO Science for Peace and Security Series - E: Human and Societal Dynamics
Editor: B.K. Wiederhold
November 2011, 224 pp., hardcover
ISBN: 978-1-60750-796-3
Price: €120 / US$174

It has been shown that those who have served in both combat missions and peacekeeping operations are at increased risk for Traumatic Brain Injury (TBI). Research suggests that this may result from their “wounds of war.” Some wounds may be “invisible,” such as depression, stress, and chronic pain, while others, such as physical disabilities, are more obvious. In February 2011, 35 scientists and representatives from NATO and partner countries met in Vienna, Austria for a three-day NATO Advanced Research Workshop entitled “Wounds of War: Coping with Blast-Related Traumatic Brain Injury in Returning Troops.”

The aim of this publication, which presents papers from that workshop, is to critically assess the existing knowledge and to identify directions for future actions. The book addresses four key questions:
1. Characterization of TBI: Which characteristics make up and help to classify TBI?
2. Diagnosis and Assessment Issues Surrounding TBI: Which methods are used to diagnose and assess TBI?
3. Treatment of TBI: What are the latest treatment and therapy opportunities for soldiers after they have been diagnosed with TBI?
4. Quality of Life: How are the lives of TBI patients affected and in what ways can their quality of life be increased?
Military posttraumatic stress disorder (PTSD) is a common and disabling consequence of war, terrorism and natural disasters which presents an increasing problem for service men and women around the world. It has been shown that those who serve in both combat missions and peacekeeping operations are at greater risk of developing PTSD as a result of the "wounds of war." These wounds may take the obvious form of physical disabilities, but "invisible" wounds, such as depression, anxiety, stress and chronic pain may also lead to an increased risk of PTSD. This book presents full papers, focused on the key presentations from the NATO Advanced Research Workshop, Wounds of War: Coping with Posttraumatic Stress in Returning Troops, held in October 2009. These papers critically assess existing knowledge in the field and identify directions for future action. The book addresses the five key issues of PTSD: vulnerability, diagnosis and assessment, prevention, treatment and associated disorders. While PTSD may be an invisible illness, its effects are certainly not invisible. Countries must work together to develop prevention and treatment strategies which ensure that service men and women are able to assimilate back into society to lead productive lives and enjoy the freedom they fought to protect. The purpose of this book is to contribute to this process.

Lowering Suicide Risk in Returning Troops: Wounds of War discusses the topic of increased suicide risk in service men and women around the world. Research has shown that those who have served in both combat missions and peacekeeping operations are at an increased risk for suicide. Research suggests that this may result from their "wounds of war." Some wounds may be more "invisible" such as depression, posttraumatic stress disorder, and chronic pain, while others are more visibly apparent such as physical disabilities. Whatever the wound, however, it seems they may all lead to an increased risk of suicide. In this book, many aspects of military suicide and how to effectively deal with this issue are discussed. Specifically, some of the questions raised are: How do we detect those who are vulnerable to increased suicide risk, possibly due to a combination of genetics and past environmental insults? How do we most appropriately assess for increased risk? Once detected, how do we help to decrease that risk? Are there pre-deployment training methods we can employ to help "inoculate" individuals against increased risk? Are these in-theater and post-deployment methods most appropriate for dealing with this risk?
**FEATURES**

Glucocorticoids Enhance Extinction-based Psychotherapy in Virtual Reality

“All patients profited from the VR Exposure, but the group that received the combination of cortisol with VR exposure had a higher treatment success.”

By Dorothee Bentz et al.

Exposure therapy is a state-of-the-art treatment approach for anxiety disorders with a high success rate. During exposure therapy, a patient exposes himself systematically to the feared object (e.g. a dog) or situation (e.g. a height situation) within a therapeutic context. Apart from conventional approaches to anxiety disorder treatment, exposure to real objects or situations (in-vivo exposure) and mental exposure to imagined objects or situations (in-sensu exposure), in virtual reality (VR) exposure has become a third valuable variant.

During VR exposure patients are exposed to virtual environments, which can include any feared stimuli or display any scenario. This approach benefits the treatment of patients whose feared situations are conventionally difficult to recreate under traditional therapeutic conditions.

Despite successes in exposure-based treatment approaches, there is still room for improvement and a need for continuous research. Recently, researchers in the field have started to translate neuroscientific findings into new clinical applications. However, before these approaches can be applied in daily clinical routine, they have to be systematically tested in pre-clinical and clinical studies. Beyond the mentioned clinical benefit of VR exposure, the VR technique has certain features that make VR ideal for this kind of research.

For example, the therapist has the opportunity to expose every patient in an identical, uniform manner within the same situations as often as needed, which is essential for the standardization of experimental protocols as needed in pre-clinical and clinical studies. Additionally, the therapist has better possibilities to control unpredicted events that can occur in real environments (e.g. other fearful people) and is able to control the intensity of exposure better.

Therefore, we decided to use the VR technique in our study. We investigated if the combination of exposure with cortisol administration, a steroid hormone naturally produced in the human body during stress, would be beneficial for the treatment of patients with height phobia. For our study we created a semi-structured exposure regime that was adapted to the subjective fear of each participant during each exposure session. Patients with height phobia were exposed in a virtual height environment. Half of the participants had taken cortisol before exposure, and the other half a placebo. Our results showed that all patients profited from the VR exposure, but the group that received the combination of cortisol with VR exposure had a higher treatment success. Our study not only indicates that cortisol has the potential to augment the efficacy of exposure therapy, but also shows that the emergence of new technologies such as VR is in favor to develop new treatment approaches.

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Figure 1: Virtual Reality environment for height simulation
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Cybertherapy in Medicine - Clinical Applications to Reduce Pain and Anxiety

"Whether it is for traumatic head injuries, burn wound care, lumbar punctures or during chemotherapy treatment for children, virtual reality has many applications."

By José Luis Mosso Vázquez et al.

From the beginning of the 21st century, many authors have analysed and published reports on the benefits of applying virtual reality to medicine within clinical procedures. Whether it is for traumatic head injuries, burn wound care, lumbar punctures, or during chemotherapy treatment for children, virtual reality has many applications. The first published case report relating to the use of virtual reality within an invasive medical procedure was in 2004 by our group, beginning with upper gastrointestinal endoscopies and so on, until the introduction of virtual reality (VR) in a postoperative care unit of cardiac surgery. The end goal of this project is to demonstrate that virtual reality is a complementary tool to reduce pain and anxiety in hospitals during medical procedures including surgical procedures.

There are many reasons and justifications to use VR in hospitals. In Neonatology (0-28 days old) there are newborns who can stay in care units for days, weeks and even months, growing without contact from the outside world apart from a few hours a day where parents can visit their children. The psychological impact in growth and development during childhood is incredibly strong; this is where neurostimulation in a closed environment is a useful alternative. In infants, virtual reality has been a good resource to reduce pain and anxiety in oncology. Hunter Hoffman has also demonstrated the benefits of using virtual reality during medical rehabilitation for child burn victims. It can also be applied for postoperative cardiac surgery patients whose rehabilitation consists of mainly staying in bed under sedatives and other treatments. The application of VR not only helps psychologically, due to their severely limited movement, but also helps improve breathing. In ambulatory surgery too, vir...
“The main benefit of applying virtual reality is that, due to the reduction of pain and anxiety and its non-invasive method, it allows for reduction in medication, bed days and, especially, an increase in the well-being of patients.”

Virtual reality cannot only help reduce pain and anxiety for the patients during the operation, but also during their recovery. There are, of course, many more areas of medicine where virtual reality can be applied; gynecology and obstetrics, gastrointestinal endoscopy, pediatrics and epidural and spinal block anesthesia.

While all patients were affiliated with Instituto Mexicano del Seguro Social (IMSS) and Instituto de Seguridad y Servicios Sociales para los Trabajadores del Estado (ISSSTE), the subjects were of different gender and age, and were mostly undergoing different types of medical procedures. Despite this, the techniques used in order to measure the success of the application of virtual reality to patients remained the same. The necessary virtual reality equipment would be mounted which was followed by a nurse measuring blood pressure, heart rate and breath rate before, during and after the procedure. Next, the physicians would ask their patients on a scale of 0-10 whether or not they were feeling anxiety or pain which would occur multiple times during a procedure.

The strongest results were seen in the three main representative groups where pain and anxiety were highest, colposcopy, ambulatory surgery and postoperative care unit of cardiac surgery. While the comparative measure of pain was made before, during and after each procedure, the statistical method to measure pain was used with a scale of 0-10 (zero is no pain and 10 is a high level of pain).

In the colposcopy group that used VR, the mean pain before the procedure was 7.5 and 5.35 during. Afterwards, the difference was of 2.15, corresponding to a 28.66% in the reduction of pain. In the colposcopy group that didn’t use VR, the mean pain before was 6.43 before and 6.78 during which is a difference of 0.35, an increase of pain of 5.44% in postoperative cardiac surgery patients, a reduction of pain and anxiety by 54.5% was seen, despite the mean pain at the beginning of the procedure being 8. Despite the lower mean, 5.57, of pain for the surgical group who did not use virtual reality, a reduction of pain and anxiety at the end of the procedure was only 36.80%. With these results we can appreciate the impact the distraction of virtual reality provides the patient in order to reduce anxiety and subsequently, visceral and somatic pains that regional anesthesia can induce.

While results varied depending on age, gender, procedures, culture, diagnosis and prognosis, all in all the data showed that the reduction of pain and anxiety, the latter in particular was prominent.

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## Product Comparison Chart: Enhancing VR with Drugs

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<table>
<thead>
<tr>
<th>DRUG</th>
<th>HOW IT COULD HELP</th>
<th>VR APPLICATIONS</th>
</tr>
</thead>
</table>
| Adderall | Increases concentration on outside tasks, where it reduces self-awareness, and combat training. | - VR public speaking  
- VR combat training |
| Amphetamines | Enhance motor skills needed to learn how to drive and for combat training. | - VR driving  
- VR combat training |
| Cannabinoid CB1 receptor antagonist AM-251 (at a dose of 1.0mg/kg or higher) | May be useful in the control of nightmares and night terrors | - PTSD [prevention] |
| Cortisone/Cortisol | Decreases fear as the user undergoes exposure therapy | - Any phobia that can be treated with VR exposure therapy |
| D-cycloserine (DCS) | Decreases fear as the user undergoes exposure therapy | - Any phobia that can be treated with VR exposure therapy |
| Dextroamphetamine (D-amphetamine / Dexedrine) | Can enhance motor skills needed to learn how to drive, increase concentration for combat training / other | - VR driving  
- VR combat training |
| Donepezil (Aricept) | outside tasks.  
Ability to boost learning for combat training | - VR public speaking  
- VR combat training |
| Dopamine D2-like receptor antagonist sulpiride | Decreases fear as the user undergoes exposure therapy | - Any phobia that can be treated with VR exposure therapy |
| Endogenous Cannabinoid (eCB) breakdown and reuptake inhibitor AM404 and other eCB modulators | Decreases fear as the user undergoes exposure therapy | - Any phobia that can be treated with VR exposure therapy |
| Ephedra/ephedrine | Increases concentration on outside tasks, where it reduces self-awareness, and combat training | - VR public speaking  
- VR combat training |
| L-type voltage-gated calcium channel agonist BayK8644 | Decreases fear as the user undergoes exposure therapy | - Any phobia that can be treated with VR exposure therapy |
| Methylphenidate (Ritalin) | Increase ability for concentration on an outside task that is needed in combat training | - VR public speaking  
- VR combat training |
| Modafinil (Provigil) | Increases alertness for combat training | - VR combat training |
| Propranolol Hydrochloride | Decreases fear on past negative memories | - VR with PTSD |
| Protein synthesis inhibitor anisomycin (ANISO) injections [under research, tested only in animals] | Decreases fear as the user undergoes exposure therapy and decreases past negative memories | - Any phobia that can be treated with VR exposure therapy  
- VR with PTSD |
| Sertraline (Zoloft) | Improves reaction time and alertness, which are useful skills for driving and combat training | - VR driving  
- VR combat training |
| Transcription factor cAMP–response–element–binding protein (CREB) inhibitors [still in research] | Decreases fear on past negative memories | - VR with PTSD |
| Yohimbine | Decreases fear as the user undergoes exposure therapy | - Any phobia that can be treated with VR exposure therapy |
Annual Review of Cybertherapy and Telemedicine 2011
Advanced Technologies in the Behavioral, Social and Neurosciences
Editors: B. K. Wiederhold, S. Bouchard, and G. Riva
$167.00

Cybertherapy – the provision of healthcare services using advanced technologies – can help improve the lives of many of us, both patients and health professionals, while tackling the challenges to healthcare systems.

Virtual Healers
Brenda K. Wiederhold, Ph.D., MBA, BCIA
$24.95

Virtual Reality in the Mental Health arena is barely over a decade old. Because VR is still such a young and focused field, the members of its community have come together as a tight-knit family. In Virtual Healers, Dr. Brenda K. Wiederhold, herself a pioneer of VR, sits down in casual one-on-one interviews with more than a dozen of the top researchers of this select group.

Virtual Healing
Brenda K. Wiederhold, Ph.D., MBA, BCIA
$19.95

Along with aliens and time travel, virtual reality (VR) is often thought of as a science fiction dream. Though it was developed nearly five decades ago, the use of VR in the private sector, particularly in the field of patient care, has become a possibility only in the past decade. As programmers are creating more detailed and interactive environments, the rapid advancement of technology combined with decreasing costs has turned VR into a promising alternative to traditional therapies.

Virtual Reality Resources
By Brenda K. Wiederhold, PhD, MBA, BCIA
$19.95

We, at the Interactive Media Institute, realized early on that it was relatively difficult for professionals wanting to break into the Virtual Reality (VR) field to locate relevant information. While the material was out there, there was no clear organizational structure or database to link it. To solve this problem, we have put together Virtual Reality Resources, a relevant compilation for researchers and clinicians alike.

CyberTherapy Conference Archives 1996-2005
A Collection of all abstracts from the past 10 years of CyberTherapy
By Brenda K. Wiederhold, PhD, MBA, BCIA
$29.95

A decade ago, CyberTherapy, then still in its infancy, only existed as a specialized Virtual Reality and Behavioral Healthcare Symposium at the Medicine Meets Virtual Reality (MMVR) Conference. It is now clear that in 1996, we had only begun to realize what promise might lie ahead for both VR technology and the CyberTherapy Conference.

iACToR Resources
http://www.vrphobia.com/products.htm - 1-866-822-VRMC - frontoffice@vrphobia.com
You can only make the journey with the knowledge of people you meet on the journey. There are designated corridors and they don’t all meet in a square ... the neurologists have societies for neurology, the psychiatrists have it for psychiatry ... there is no cross-fertilization. This is what drove me to set up the European Brain Council.”
**ASK THE EXPERT**

Mary Baker

Epilepsy UK, we formed the European Parkinson’s Disease Association that brought together nine European countries and currently has 45 members. The first step was to bring together with the common disease, the glue. The European Commission doesn’t want to talk about a single disease. They do not want to speak about Parkinson’s because it is part of Brain Disease. So it seemed logical to bring all the brain diseases together. That was the Federation of the Neurological Associations which started to work well with the European Commission as it dealt with one organ over a disease. But that does not satisfy everyone. Now we created the European Brain Council (EBC), which includes patients living with neurological disorders, patients living with mental illness, neuroscientists, neurosurgeons, neurologists, patients mental illness, pharmacology, biotech, health insurance and a group of MEPs who are interested in the area. It starts to bring a whole sector together all pushing for increasing money for brain research, listening on how to deal with regulators and how you deal with the payers. The patient groups have now become a sector of society. Patients are not a group; society is what we belong to. This is a society who happens to be living and involved with the brain. We have progressed much further in dealing with the European Commission and we are now a consultant for DG Research and with the upcoming Horizon 2020 program. It’s like building a choir. You cannot have a choir of all sopranos. With one voice, you will get a lot further.

**BKW:** How can we ensure brain research receives the attention and financial support it deserves?

**MB:** This is where we have to collect the data as no one fully understands the costs of the disease. The World Health Organization and the United Nations has designated four diseases to receive the top priority: cancer, cardiovascular, COPD and diabetes. But there is no mention of the brain. But brain should be running the management of those four diseases. How can I prevent this? Should I do some rehabilitation? When should I take my medication? The brain was totally left out. The EBC gathered data in 2004 and again in 2010 data and launched its results in the European Parliament in October 2011. The cost of brain diseases across Europe is just under 800 billion Euros. This is more than cancer, diabetes and cardiovascular diseases combined. This is because those diseases kill whereas brain diseases go on and on. I have tried to argue that the organizations measure the importance of illness by death rate but this totally leaves out the costs of the illnesses and by far the biggest drain of resources is the brain diseases. I am not arguing that they are more important but that they are more costly. If you don’t attend to these costs, they will drain resources from everything else. The cost of death is 0 but what is the cost of 30 years living with Parkinson’s and other long-term illnesses?

**BKW:** For those who have suffered a brain injury, what isn’t currently being done that needs to be done?

**MB:** Prevention. Why are we not taking care of the brain? Why are children still on bicycles without helmets? Why are we neglectful of the impact on alcohol on brain? Why are the universities, who are treasuring our brightest who may one day become our neuroscientists, encouraging students with Fresher’s week where they drink and drink and drink? We don’t do enough about prevention. It all relates to social behavior. We know alcohol is harmful and statistics show that it is responsible for 10% of road accidents and 25% of murders. We need to raise awareness amongst society of the importance of adopting healthy lifestyles.

**BKW:** Do you have any predictions on new trends for healthcare and technology for the next decade?

**MB:** Data analysis used to take forever and now there is technology where it can be used so swiftly. DNA sequencing, for example, used to take a very long time but now it has been made much faster because of technology. Technology will help us have a better understanding of the organs which will help speed the progress of health care.

**BKW:** Anything else you would like to add?

**MB:** Don’t believe however clever you are that one specialty or person has the definitive answer. If we come together, share ideas and are willing to break barriers with the confidence of other disciplines, we will start to move forward.”
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Conquering Panic, Anxiety, & Phobias
Achieving Success Through Virtual Reality and Cognitive-Behavioral Therapy
By Dr. Brenda K. Wiederhold, PhD, MBA, BCIA

This book is written as a starting point toward helping the large portion of our population that suffers from anxiety disorders to overcome their fears and control their anxiety. It is a resource to enable those suffering from anxiety to take control of their lives and become an active participant in their own recovery.

This book is essentially divided into two parts: a discussion of anxiety and its physical and emotional effects on sufferers. While Virtual Reality Therapy is described, its use is not necessary in order to follow the suggestions in this book. The lessons and worksheets included can help in a variety of areas, not just anxiety, but anger, mild depression, and feelings of helplessness.

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In this and in the last issues we reviewed in this journal different applications of virtual reality (VR) in medicine. All of these researchers share a common vision of what virtual reality is: a collection of technologies that allow people to interact efficiently with 3D computerized databases in real time using their natural senses and skills (2). This definition lacks any reference to head mounted displays and instrumented clothing such as gloves or suits. In fact, less than 10% of VR health care applications in medicine are actually using any immersive equipment.

However, if we focus our attention on behavioral sciences, where immersion is used by more than 50% of the applications, VR is described as an advanced form of human-computer interface that allows the user to interact with and become immersed in a computer-generated environment in a naturalistic fashion.

These two definitions underline two different visions of VR.

Clinical psychologists and rehabilitators use VR to provide a new human-computer interaction paradigm in which users are no longer simply external observers of images on a computer screen but are active participants within a computer-generated three-dimensional virtual world. The key characteristics of virtual environments for these professionals are both the high level of interaction control using the tool without the constraints usually found in other computer systems, and the enriched experience provided to the patient.

For physicians, and surgeons, the ultimate goal of VR is the presentation of virtual objects to all of the human senses identical to their natural counterpart. As more and more medical technologies become information based, it will be possible to represent a patient with higher fidelity to a point that the image may become a surrogate for the patient — the medical avatar. In this sense, an effective VR system should offer real-like body parts or avatars that interact with external devices (e.g. surgical tools) and drugs as near as possible to their real models.

Using medical avatars, the researchers hope to predict the biological effects of the various drugs in the hope of fine-tuning their components and ideally, eliminating the costs of unsuccessful trials before they are even synthesized.

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Presenting the Proceedings of

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C&R in Belgium

Brussels, Europe’s capital, has developed a focus to enhance advanced technological healthcare, locally and globally. The European Commission envisages SMEs as drivers of new innovation and growth within this sector and have thereby set out policies to help SMEs to develop and grow.

Belgium, like many Northern European Countries, is regarded as having a very high standard of living. Belgium has a complex history as a relatively new country with three defined communities; the Flemish region in the north (Dutch speaking), the Walloon region in the south (French and German speaking) and the Brussels region (bilingual). These three communities, defined by their language, have political powers over areas in education, culture and ‘social matters’ such as families and healthcare. With its capital Brussels, also the capital of the European Union, there are numerous policymakers, funding agencies, and research projects for the healthcare sector on an international scale.

Brussels, Europe’s capital, has increasingly focused on ATH, locally and globally. The European Commission sees SMEs as drivers of new innovation and growth of the ATH sector and has set out policies to assist SMEs in their growth and development. On the Woluwe Saint Lambert campus of the Université Catholique de Louvain (UCL), the Brussels Life Science Incubator (BLSI) opened in December 2011, to provide a dynamic environment for start-up SMEs and business leaders active in the field of biotechnology, medical devices, and IT solutions for the Health Sector. BLSI helps start-ups and SMEs to develop new activities by providing the right environment and personalized support services. Two such Advanced Technology Healthcare SMEs housed in BLSI are Esperity and Virtual Reality Medical Institute (VRMI).

Virtual Reality Medical Institute (VRMI)

One of the first companies selected for inclusion in the incubator was Virtual Reality Medical Institute (VRMI). VRMI is a Belgian SME with expertise in simulation technologies in three main areas: 1) treating patients with stress, anxiety, and trauma, 2) training for military medical and civilian first responder populations, and 3) enhancing medical educational programs. A relatively new start-up, VRMI has established affiliates in both China and the U.S.

“The new era in medicine has arrived and the empowered patient is born.”
Using a Combined Communications Platform of an annual international conference, specialized workshops, clinician training courses, a peer-reviewed scientific journal, a quarterly magazine, and a website information portal as tools to inform and educate the general public, policymakers, funding agents, industry and academia. In addition, VRMI has a private clinic at BLSI for patient care to transition protocols and clinical products developed in the laboratory setting into actual clinical use. Having been involved in R&D projects in Europe, Asia, and the U.S. for the past 25 years, the principals of VRMI have won over 50 competitive government contracts and are now actively involved in marketing the developed products and protocols.

VRMI is currently involved with a particularly high profile project funded by DG-CONNECT entitled INTERSTRESS. INTERSTRESS is working with a new e-Health concept called Interreality and is porting physiology and virtual reality to mobile platforms to provide easier access to stress prevention and stress management tools for individual citizens. Selected as a 2012 winner for the World Summit Award on mHealth, INTERSTRESS will complete its clinical and marketing trials in December 2013.

(http://www.vrphobia.eu)

**Esperity**

Esperity, also based at the BLSI, is a new start-up SME providing a platform for cancer patients to report their treatment outcomes and to connect with other patients similar to themselves. It is the aim of Esperity to dig into this data to find correlations between influencing variables on cancer treatment outcome. Patients all over the world can enter data such as cancer type, cancer subtype, treatment, medical history, medication schemes, side effects and quality of life indicators. With the use of Microsoft cloud technology, patients’ data can be scaled and relocated depending on their location. By analyzing the data of the users, certain patterns will become visible. For example, patients with a specific type of breast cancer taking an anti-diabetic drug might report totally different side effects and quality of life indicators compared to patients taking an anti-hypertension drug. Being based at BLSI provides the environment and location to develop the SME to a wider market. (http://esperity.com)

"The EU is beginning to focus on the involvement of SMEs in the valorization of research potential with international cross-sectional collaboration, making Belgium an attractive place for high tech medical SMEs.”

There is a technological shift taking place within healthcare and technology, and this is increasingly becoming accepted by mainstream patients. Together with the increased possibilities that modern technology offers, a huge boom of medical data is to be expected. Interpretation of all this information is key, together with using this information for feedback to patients to maximize the effectiveness of technology. The ‘ease-of-use’ of future technologies is vitally important...
to meet the requirements of the consumers. Cloud computing will hopefully bridge the gap in access to new technologies whilst reducing investment costs making a more accessible entry point.

Centre of the EU

With Belgium being situated at the heart of Western Europe and Brussels its Capital, the main European institutions, major companies and research institutes all over the world have delegates in and around Brussels. One group with headquarters in Brussels is the International Association of CyberPsychology, Training, & Rehabilitation (iACTOR), which is a members-based international non-profit association incorporated in Belgium. iACToR is designed to promote Virtual Reality and other advanced technologies as adjuncts to more traditional forms of therapy, training, education, and rehabilitation. It also investigates how new social networking tools are impacting (positively and negatively) individual behavior, interpersonal relationships and society. iACToR members are working to develop a “roadmap” for the future of this rapidly growing area and participate in annual conferences and online forums to share ideas and consolidate experiences. (http://iactor.ning.com)

Being located in Belgium gives institutions the benefit of easier access to an international stage. Projects are not limited to which country they are located in and can find the best researchers within the EU rather than their home state. Increasing demands on healthcare have created a need for an overall shift from institutional healthcare settings to everyday environments, and from treatment to a preventive approach based on new personalized healthcare technologies. Using new technologies will help the treatment of patients as well as cutting ever increasing costs. One area that has empowered the patient is Virtual Reality, which is increasingly being researched and applied within the healthcare field.

The Strategic Approach for the EU for 2008-2013 stated that ‘health is the greatest wealth’ and that ‘health is important for the wellbeing of individuals and society, but a healthy population is also a prerequisite for economic productivity and prosperity’. Esperity and VRMI, both located at the Brussels Life Science Incubator (BLSI), have the benefits of being closely linked to UCL, as well as outstanding research facilities throughout Belgium. Networking events organized by BLSI also help SMEs establish access to funding agencies such as Innoviris and IWT that promote collaboration between these research facilities and SME’s.

Having access to the European Commission and EU funds enables SMEs to push forward research for Advanced Technology Healthcare as well as providing the basis for international collaborations. These technologies enable treatments using Virtual Reality, the Internet, and Cloud Computing to be accessible whenever and wherever, creating a greater link between patient and physician.

Moving Forward

As Europe is already pushing for stronger collaboration between academic/research institutes and SMEs in its Horizon 2020 framework, many hope the fruits of this initiative will be harvested soon, with a positive effect on the European economy. Being based at the Brussels Life Science Incubator optimizes SME’s abilities to collaborate with high quality research facilities locally and internationally with enhanced access to relevant European departments and Commissions. Designed to help new startups with some of the most difficult issues they face by providing workspace, support services, and networking opportunities, entrepreneurs have more time available to focus on their subject matter expertise and the enthusiasm needed to grow their businesses.

Europe, as does the U.S., agrees that small business innovation remains one of the keys to moving our countries forward.

Sources:

Personal communication with Mitchell Silva, World Health Organization (WHO), Brussels Life Sciences Incubator (BLSI) and Europa.eu
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