USC School of Pharmacy — Department of Regulatory and Quality Sciences | SC CTSI | USC School of Pharmacy — DK Kim International Center for Regulatory Science

ONLINE REGISTRATION NOW OPEN!

Regulatory Science Symposium

Emerging Technologies in the Medical Device Industry

Friday, Sept. 23, 2022 | 9AM - 4PM PDT | Online via Zoom

Agenda

9:00 AM PDT	**Introduction** *Eunjoo Pacifici, PharmD, PhD* USC, SC-CTSI, School of Pharmacy I Chair & Associate Professor, Dept. of Reg. & Quality Sciences Associate Director, DK Kim International Center for Regulatory Science
9:30 AM PDT	**What is Digital/AI/Machine Learning? How is It Used?** *Steve Thompson, BS* ValGenesis Inc. | Director Industry Solutions
10:15 AM PDT	**Break**
10:30 AM PDT	**Clinical Virtual Reality: Seven Ways that Virtual Reality Will Change the World of Mental Healthcare!** *Albert "Skip" Rizzo, PhD* USC Davis School of Gerontology and USC Keck School of Medicine Dept. of Psychiatry & Behavioral Sciences I Research Professor
12:00 PM PDT	**Lunch**
1:00 PM PDT	**Regulatory Framework for the Digital World** *Steve Thompson, BS* ValGenesis Inc. | Director Industry Solutions
2:00 PM PDT	**Use of AI in Drug Development** *Megan Doyle, JD, MPH* Amgen | Director, Global Regulatory and R&D Policy
3:00 PM PDT	**Break**
3:15 PM PDT	**Cybersecurity** *Jay Nayar, MS, RAC* Google | Regulatory Affairs
4:30 PM PDT	**Wrap-Up** *Susan Bain, DRSc* USC, School of Pharmacy I Assistant Professor, Dept. of Reg. & Quality Sciences

Regulatory Science Symposium:

Emerging Technologies in the Medical Device Industry

Speaker Bios

Eunjoo Pacifici, PharmD, PhD, is the Chair and Associate Professor of Regulatory and Quality Sciences and Associate Director of the DK Kim International Center for Regulatory Science at USC. Dr. Pacifici received a BS in Biochemistry from the University of California Los Angeles followed by a PharmD and PhD in Toxicology from USC. She conducted her graduate research in the laboratory of Dr. Alex Sevanian in the Institute for Toxicology where she studied the mechanism of oxidative damage and repair in endothelial cell membrane. Before returning to USC as faculty, Dr. Pacifici worked at Amgen and gained experience in conducting clinical research with a special focus on the Asia Pacific and Latin America regions. She initially worked in the clinical development group managing U.S. investigational sites and central laboratories and then went on to work in the Asia Pacific / Latin America group interfacing with local clinical and regulatory staff in Japan, the People's Republic of China, Taiwan, and Mexico. She represented regional clinical and regulatory views on therapeutic product development teams and led satellite task forces in order to align local efforts with U.S. activities. Her additional professional experiences include community pharmacy practice in various settings and clinical pharmacy practice at the Hospital of the Good Samaritan in Los Angeles. Her current focus is on developing the next generation of regulatory scientists and pharmacy professionals with the knowledge, tools, and skills to expedite the development of innovative, safe, and effective biomedical products. epacific@usc.edu

Steve Thompson, BS, is the Director Industry Solutions at Valgenesis Inc. He holds a Bachelor of Science in Computer Information Systems and Computer Science from DeVry University and is certified by the Parenteral Drug Association (PDA) as a Computer Systems Auditor. He has worked in Life Sciences for over 20 years and have audited hundreds of companies globally. He is a published author, board member of for the Pacific Regional Chapter of the Society of Quality Assurance, on the Editorial Advisory Board for a peer-reviewed industry journal, recipient of the APEX 2020 "Award of Excellence" in the category of "Writing." He often shares his expertise about the roles of digital learning, artificial intelligence, and machine learning in the medical product industry at USC as a guest lecturer. Steve.thompson@valgenesis.com

Albert "Skip, Rizzo, PhD, is a Research Professor at the USC Keck School of Medicine, Department of Psychiatry and Behavioral Sciences and at the USC Davis School of Gerontology. He is also the Director for Medical Virtual Reality at the USC Institute of Creative Technologies. He holds a PhD in Clinical Psychology from Binghamton University and MS in Experimental Psychology from University of New Orleans. He conducts research on the design, development, and evaluation of virtual reality (VR) systems targeting the areas of clinical assessment, treatment rehabilitation and resilience. This work spans the domains of psychological, cognitive, and motor functioning in both healthy and clinical populations. In the past, he received the American Psychological Association's 2010 Award for Outstanding Contributions to the Treatment of Trauma for his work related to virtual reality-based exposure therapy to treat PTSD. His current work involves the design of virtual reality or VR scenarios to address social and vocational interaction in persons with autistic spectrum disorder. He is senior editor of the MIT Press journal, Presence: Teleoperators and Virtual Environments. He also sits on several editorial boards for journals in the areas of cognition and computer technology (Cognitive Technology; Journal of Computer Animation and Virtual Worlds; Media Psychology) and is the creator of the Virtual Reality Mental Health Email Listserve (VRPSYCH). rizzo@ict.usc.edu

Megan Doyle, JD, MPH is the Director of Global Regulatory and R&D Policy at Amgen Inc. She received her JD from Georgetown University Law Center, MPH from John Hopkins, and a bachelor's in Journalism from George Washington University. She possesses over a decade of legal experience, advising on matters pertaining to the regulation of drugs, medical devices, combination products, and in vitro diagnostics. She spent seven years at a medical device practice at Hogan Lovells before joining Amgen as a Senior Counsel for Health Regulatory. She also served as the law department companion diagnostic lead, advising on the co-development process for teams developing targeted policies that require a companion diagnostic. In her current role as Director, she is the Global Policy Lead for Diagnostics, Digital Health, and Combination Products. For the past 2+ years, she shares her expertise regarding FDA regulation of medical devices as a guest speaker at John Hopkins Bloomberg School of Public Health. Medoyle@amgen.com

Susan Bain, DRSc is an Assistant Professor of Regulatory and Quality Sciences at USC and formerly a Professor of Practice and Program Director for Clinical, Regulatory and Quality at Keck Graduate Institute's (KGI) and Adjunct Professor of Practice and Concentration Coordinator for Clinical and Regulatory in KGI's School of Pharmacy. She received a doctorate of regulatory science, a Master of Science in regulatory science from USC and a Bachelor of Science in biological science from Cal Poly, Pomona. She also holds a graduate certificate in effective supervision from Cal Poly Pomona. She is an accomplished quality and regulatory professional with experience in the medical device, pharmaceutical, and biotechnology industries. She has a diverse regulatory compliance background in a broad range of FDA-regulated industries. Her most recent corporate experience includes serving as a Vice President of Quality/Regulatory Assurance and Operations at medical device company and has held various management positions in Quality Control/Assurance and Regulatory Affairs over the past 25 years with firms including Baxter Healthcare, Grifols, Medegen, Inc., Peregrine Corporation, and Watson Pharmaceuticals. Additionally, Susan also worked at the FDA as an Investigator, focusing on drugs and medical devices. She currently is a member of the Orange County Regulatory Association (OCRA), Drug Information Association (DIA), Parenteral Drug Association (PDA), Association of Graduate Regulatory Educators (AGRE), and Regulatory Affairs Professionals Society (RAPS). bain@usc.edu

Regulatory Science Symposium

Emerging Technologies in the Medical Device Industry

Introduction

Eunjoo Pacifici, PharmD, PhD
Chair and Associate Professor, Regulatory and Quality Sciences
Associate Director, DK Kim International Center for Regulatory Science

UC•IRVINE ICTS from lab to life. UCLA CTSI Grant #UL1TR000124 USC School of Pharmacy DK Kim International Center for Regulatory Science SC CTSI

SC CTSI Clinical Research Support (CRS)

Lily Jara, BS
Clinical Research Supervisor, COVID-19 Biorepository Project Manager, CRS

Contact Information:
crs@sc-ctsi.org

A single stop for accessing all services an investigator and research team needs to develop, activate, conduct, and report results for human subject research studies

Initial focus on investigator-initiated trials (non-cancer)

- **Services:**
  - **Clinical research coordinators for hire**
  - **Research navigation**
  - **Recruitment support**
  - **Budget preparation support**
- **Clinical Trials Unit (CTU):**
  - **Skilled research and nursing staff**
  - **Services to support highly-complex human subjects research studies**
  - **Specimen processing lab**
- **Voucher program:**
  - **Awards up to $3,000 to generate new data for development of clinical and/or community research projects**

https://sc-ctsi.org/about/groups/clinical-research-support

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DK Kim International Center for Regulatory Science

SC CTSI

Clinical Trial Quality Training Series

Chapter on Remote Monitoring now available!

1. Go to: https://uscregsci.remote-learner.net
2. Click ***create new account*** (right-hand side)
3. Type in your information and click ***Create my new account*** (bottom of page)
4. Open your email and click the link to confirm your account
5. Click ***courses*** (middle of page)
6. Scroll down and click the desired module
7. Click ***Enroll me*** (middle of page)

USC School of Pharmacy
DK Kim International Center for Regulatory Science
SC CTSI

Georgia CTSA and SC CTSI: Online Course Catalog

- Free trainings for clinical research workforce
- Free, one-time registration to the first 400 registrants
- Registration provides unlimited access to all courses and programs in the Online Course Catalog
- Participants earn a certificate or badge with contact hours upon completion of a course or program
- Contact hours can be used for CRP certification renewal
- To get started: **https://twd.ce.emorynursingexperience.com/**

SC CTSI
Clinical and Translational Science Institute

Georgia CTSA
Clinical & Translational Science Alliance

Georgia CTSA Translational Workforce Development Announces
Online Course Catalog with Free Trainings for Clinical Research Professionals

The Georgia Clinical and Translational Science Alliance (Georgia CTSA) and the University of Southern California Clinical and Translational Science Institute (SC CTSI) are collaborating on an exciting new educational venture geared toward clinical research professionals at every stage of their professional development. Through this partnership, Georgia CTSA has created a new Online Course Catalog with free course and program offerings available to clinical research professionals and principal investigators. These courses and programs are created and vetted by experts in cross-disciplinary fields such as instructional design, technology, workforce development, regulatory science, clinical and translational science, and operations.

"We are fortunate to partner with USC SC CTSI to bring such a broad offering of high-quality trainings to our clinical research professionals."
Linda McCauley, RN, PhD, Program Director of the Georgia CTSA Translational Workforce Development and Dean of the Nell Hodgson Woodruff School of Nursing at Emory University

"This joint effort between Georgia CTSA and SC CTSI will create a wonderful resource to support training and career development of clinical research professionals at all levels. It will be a game changer, especially for people working an academic setting."
Thomas Buchanan, MD, Director & Principal Investigator of the SC Clinical and Translational Science Institute

"It has been a pleasure to partner with Georgia CTSA team in our common goal to promote life-long learning for the clinical research workforce."
Eunjoo Pacifici, PharmD, PhD, Chair and Associate Professor in the Department of Regulatory and Quality Sciences and Associate Director of the DK Kim International Center for Regulatory Science at the USC School of Pharmacy

Participants earn a certificate or badge with contact hours (continuing education) from an accredited provider upon completion of a course or a program (series of courses). Contact hours can be used to meet requirements for CRP certification renewal.

Free, one-time registration to the Georgia CTSA Online Course Catalog is available to the first 400 registrants. Registration provides unlimited access to all courses and programs in the Georgia CTSA Online Course Catalog. View the Online Course Catalog to get started.

The first program, *Legal Aspects for Conducting Clinical Trials*, is comprised of six courses. Individual courses in all programs receive a certificate, and completing the program earns a badge. The second program, *Clinical Trials with Medical Devices*, is comprised of seven courses of which completion of five of the seven courses will earn a badge. Be sure to check out the dashboard features as you build your professional career.

Stay Tuned for More Courses and Programs as We Develop This Free Online Course Catalog!

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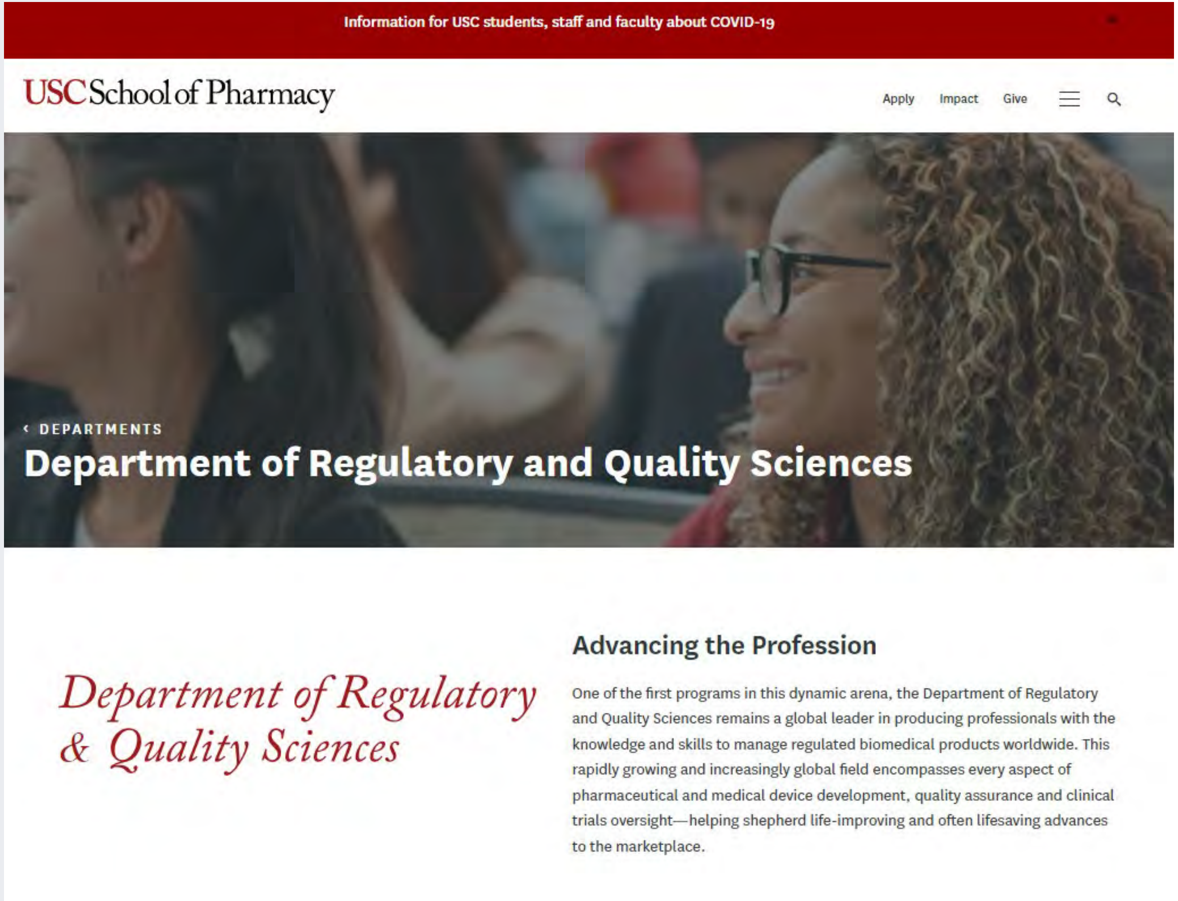
Find us on our website: https://regulatory.usc.edu/



Degree Programs

Five Graduate Streams

- DRSc
- **MS Regulatory Science**
- MS Regulatory Management
- MS Management of Drug Development
- MS Medical Product Quality

Certificates

- Food safety
- Regulatory Science
- Early Drug Development
- **Clinical Design and Management**
- Patient and Product Safety

Nancy Pire-Smerkanich
DRSc, MS

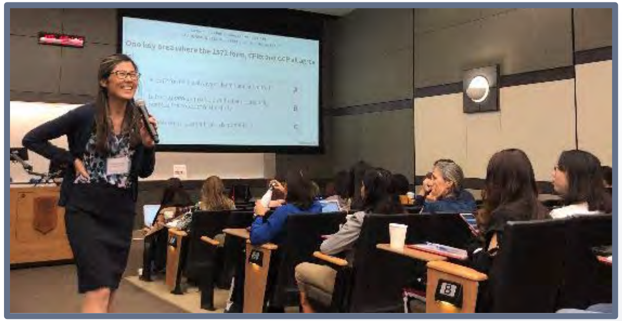
Assistant Professor
Department of Regulatory and Quality Sciences

piresmer@usc.edu

USC School of Pharmacy
DK Kim International Center for Regulatory Science

SC CTSI

Symposiums



- **2015 -** Clinical Trial Hurdles
- **2016 Spring** - Clinical Trial Startup
- **2016 Fall** - Monitoring and Auditing
- **2017 Spring** - Clinical Trials in Special Populations
- **2017 Fall** - Clinical Trials in Era of Emerging Technologies and Treatments
- **2018 Spring** - Regulatory Aspects of Clinical Trial Design
- **2018 Fall** - Pharmacovigilance and Safety Reporting
- **2019 Spring** - Patient-Centered Drug Development and Real World Evidence/Data
- **2019 Summer** - Clinical Trials with Medical Devices
- **2019 Fall** - Legal Aspects of Conducting Clinical Trials
- **2020 Spring** - Quality by Design in Clinical Trials
- **2020 Fall –** Diversity in Clinical Trials in the Time of COVID-19
- **2021 Spring** – Clinical Research Career Pathways (half-day)
- **2021 Spring** – Principles of Global Clinical Research for Medical Devices
- **2021 Fall** – Innovation to Translation: Role of Genomics in Medical Product Development
- **2022 Spring** – Make Informed Decisions: Key Statistical Principles to Clinical Trial Design
- **2022 Fall** – Emerging Technologies in the Medical Device Industry
- **2023 Spring** - TBD

Symposium recordings are easily accessible for viewing on the SC CTSI's online educational library *https://sc-ctsi.org/training-education/courses?audience=researchProfessionals*

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Presented by the USC School of Pharmacy International Center for Regulatory Science and the Southern California Clinical and Translational Science Institute

This certifies that

Before the end of today's symposium, you will receive a link to take the program evaluation.

Follow this link to the Survey:
Take the Survey

Please complete the program evaluation to receive a certificate of completion by Friday, October 7, 2022.

Eunjoo Pacifici, PharmD, PhD
Director
International Center for Regulatory Science

Thomas A. Buchanan, MD
Director
Southern California Clinical and Translational Science Institute

USC School of Pharmacy
DK Kim International Center for Regulatory Science

SC CTSI

Thank You!

www.sc-ctsi.org
Phone: (323) 442-4032
Email: info@sc-ctsi.org
Twitter: @SoCalCTSI

USC School of Pharmacy
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regulatory.usc.edu
Phone: (323) 442-3521
Email: regsci@usc.edu
Facebook: @RegSci

Valgenesis.com

Digital | Artificial Intelligence | Machine Learning

What are they, and *How* are they used

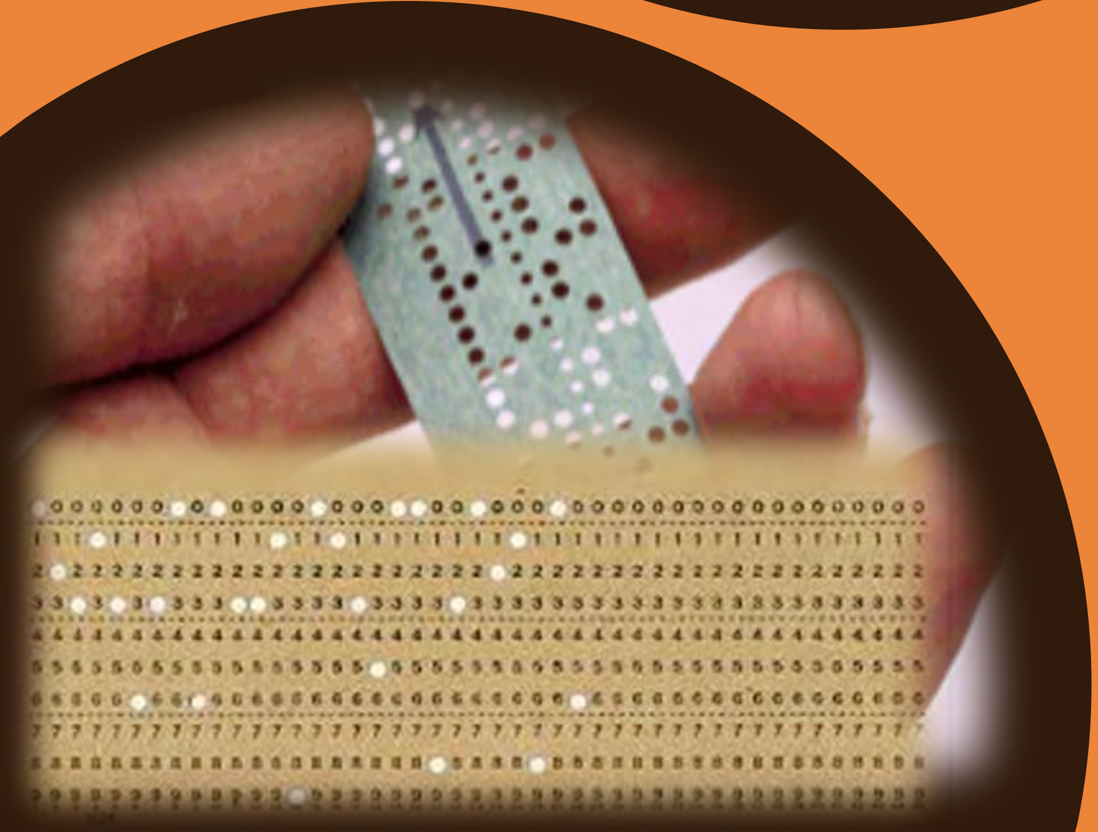
27 AUG 2021

Steve Thompson, Director Industry Solutions

ValGenesis VLMS
The de facto standard for

100%
PAPERLESS
VALIDATION

ValGenesis, Inc., 395 Oyster Point Boulevard, Suite 228, South San Francisco, CA 94080 Phone 510 445 0505



DIGITAL

ASCII: *what the computer understands*

```
L = 076
l = 108
1 = 049
O = 079
o = 111
0 = 048
```

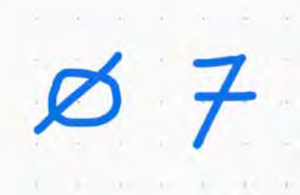
076	114	4C	0100 1100	L
079	117	4F	0100 1111	O

For lowercase letters, add 32 to uppercase value
Subtract 32 to go from lowercase to uppercase

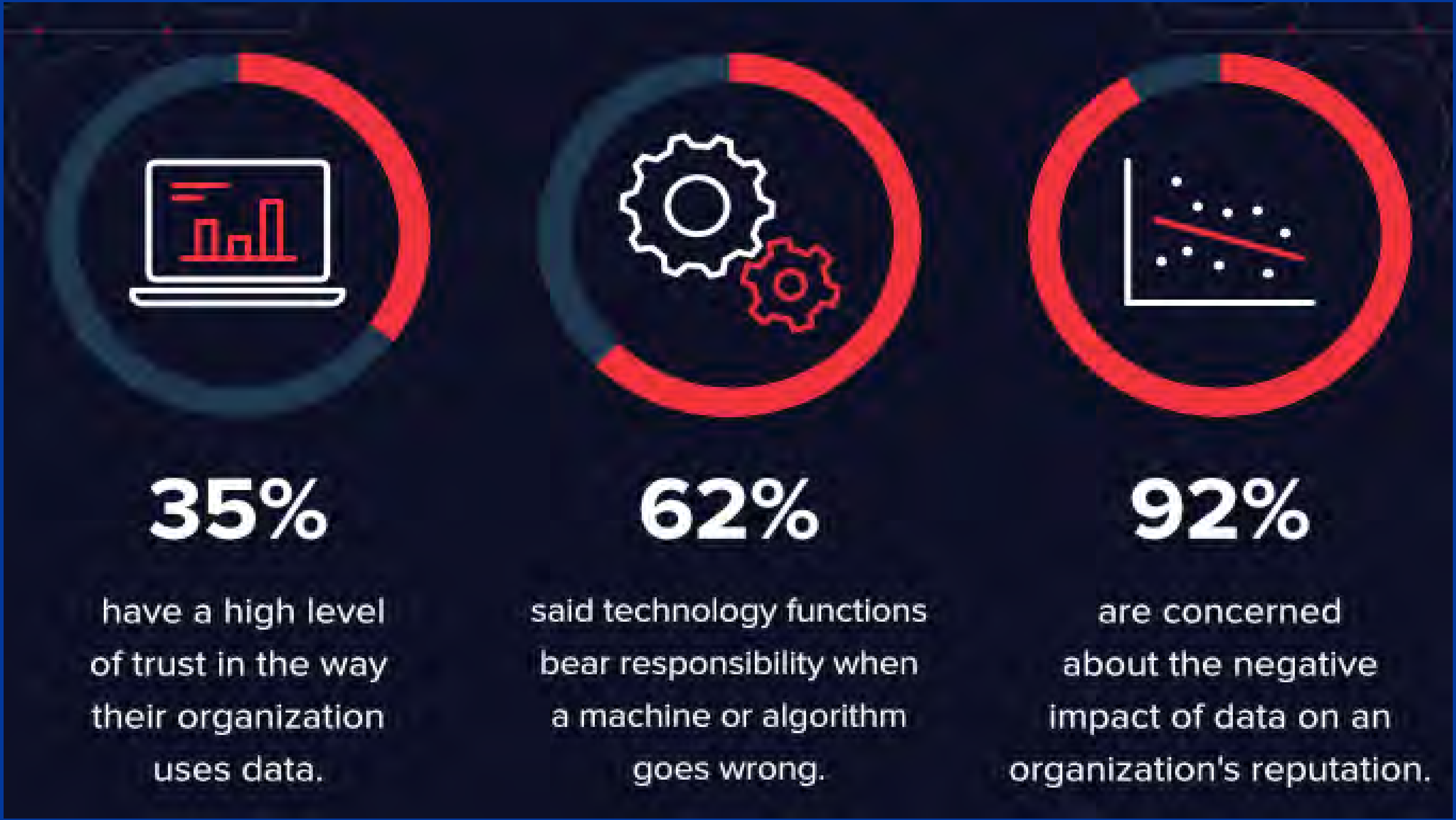
048	060	30	0011 0000	0
049	061	31	0011 0001	1

ASCII Code: Character to Binary

0	0011 0000	O	0100 1111	m	0110 1101
1	0011 0001	P	0101 0000	n	0110 1110
2	0011 0010	Q	0101 0001	o	0110 1111
3	0011 0011	R	0101 0010	p	0111 0000
4	0011 0100	S	0101 0011	q	0111 0001
5	0011 0101	T	0101 0100	r	0111 0010
6	0011 0110	U	0101 0101	s	0111 0011
7	0011 0111	V	0101 0110	t	0111 0100
8	0011 1000	W	0101 0111	u	0111 0101
9	0011 1001	X	0101 1000	v	0111 0110
A	0100 0001	Y	0101 1001	w	0111 0111
B	0100 0010	Z	0101 1010	x	0111 1000
C	0100 0011	a	0110 0001	y	0111 1001
D	0100 0100	b	0110 0010	z	0111 1010
E	0100 0101	c	0110 0011	.	0010 1110
F	0100 0110	d	0110 0100	,	0010 0111
G	0100 0111	e	0110 0101	:	0011 1010
H	0100 1000	f	0110 0110	;	0011 1011
I	0100 1001	g	0110 0111	?	0011 1111
J	0100 1010	h	0110 1000	!	0010 0001
K	0100 1011	I	0110 1001	'	0010 1100
L	0100 1100	j	0110 1010	"	0010 0010
M	0100 1101	k	0110 1011	(	0010 1000
N	0100 1110	l	0110 1100	)	0010 1001
				space	0010 0000



SOURCE: Varonis

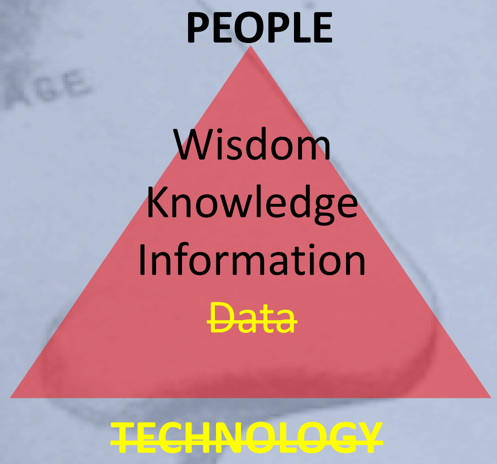


People vs
Systems

Analog Digital

Humans have perspectives and opinions

- Humans are unpredictable
- Software is created by human(s) who have perspective, right or wrong
- Oversight & testing is crucial
  - You can't *validate* a human
  - People are inconsistent and may be unaware of their actions
- People aren't good with tedious tasks and large data sets

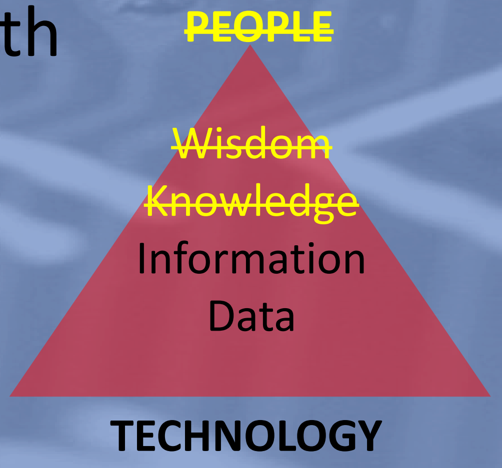


Technology

System perspective

Systems don’t have perspective

- Systems have a program they execute
- Program (software) is created by human(s) who have perspective, right or wrong
- Oversight and testing is crucial
  - *Validated* to ensure consistent intended performance
  - Once validated, system will execute as designed (right or wrong)
- Technology systems are great at processing tedious tasks with volumes of data



Hybrid perspective

Hybrid is the best of both worlds

But we must know and respect the other operates

SYSTEMS

Designed
Developed
Programmed
Data

PEOPLE

Born
Taught
Perceive
Information & Knowledge

PEOPLE

Wisdom
Knowledge
Information
Data

TECHNOLOGY

AI

Artificial Intelligence

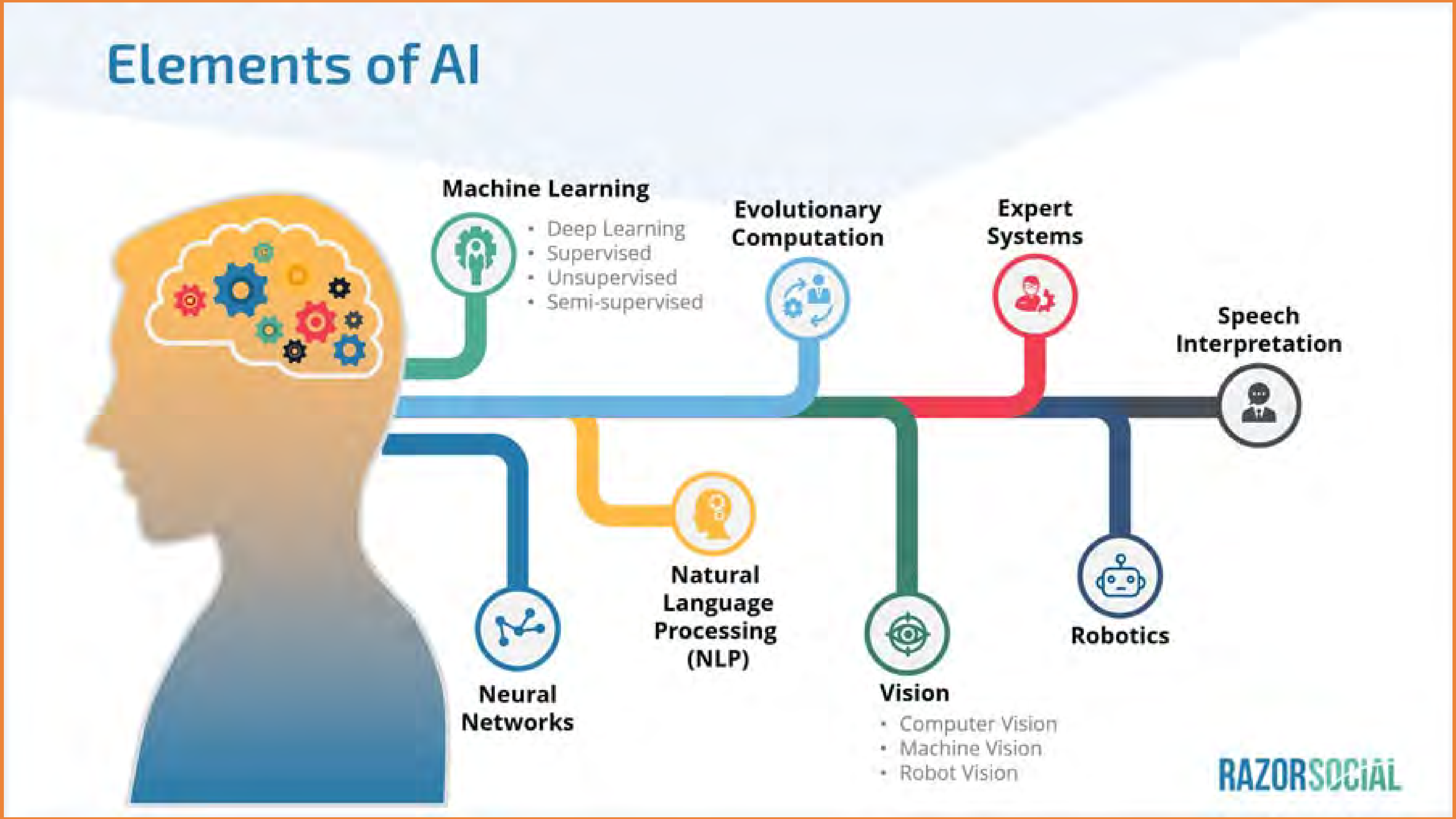
AI

“

Artificial Intelligence
is when a machine displays
<u>some</u> human-like
intelligence

”

SOURCE: RazorSocial.com



SOURCE: RazorSocial.com

AGI

“Artificial General Intelligence

The hypothetical ability of an
intelligent agent to understand
or learn any intellectual task that a human being can

It is a primary goal of some artificial intelligence research
and a common topic in science fiction”

SOURCE: Wikipedia

AGI

HAL 9000

IBM

VMS

WNT

Presenter will bring video for this slide

SOURCE: YouTube

ML

Machine learning

- **Method of data analysis**
- **Automates analytical model building**
- Branch of artificial intelligence based on the idea that systems can:
  - Learn from data,
  - identify patterns, and
  - make decisions
  - *with minimal human intervention*

SOURCE: SAS.com.

Supervised learning

Dataset observations are labeled
Algorithms learn to predict output from input

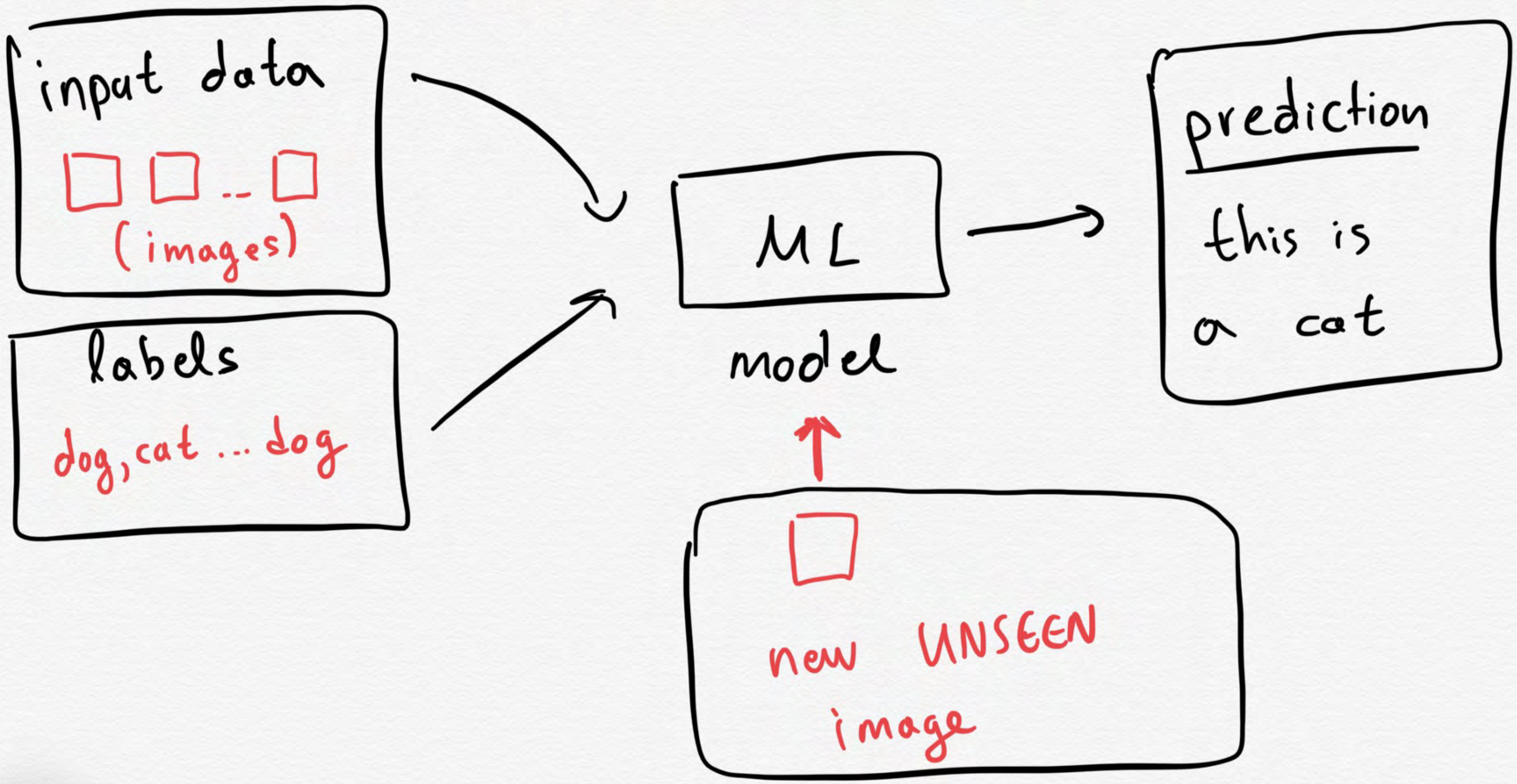
Semi-supervised learning

Dataset observations are unlabeled
Algorithms learn to inherent structure from the input

Unsupervised learning

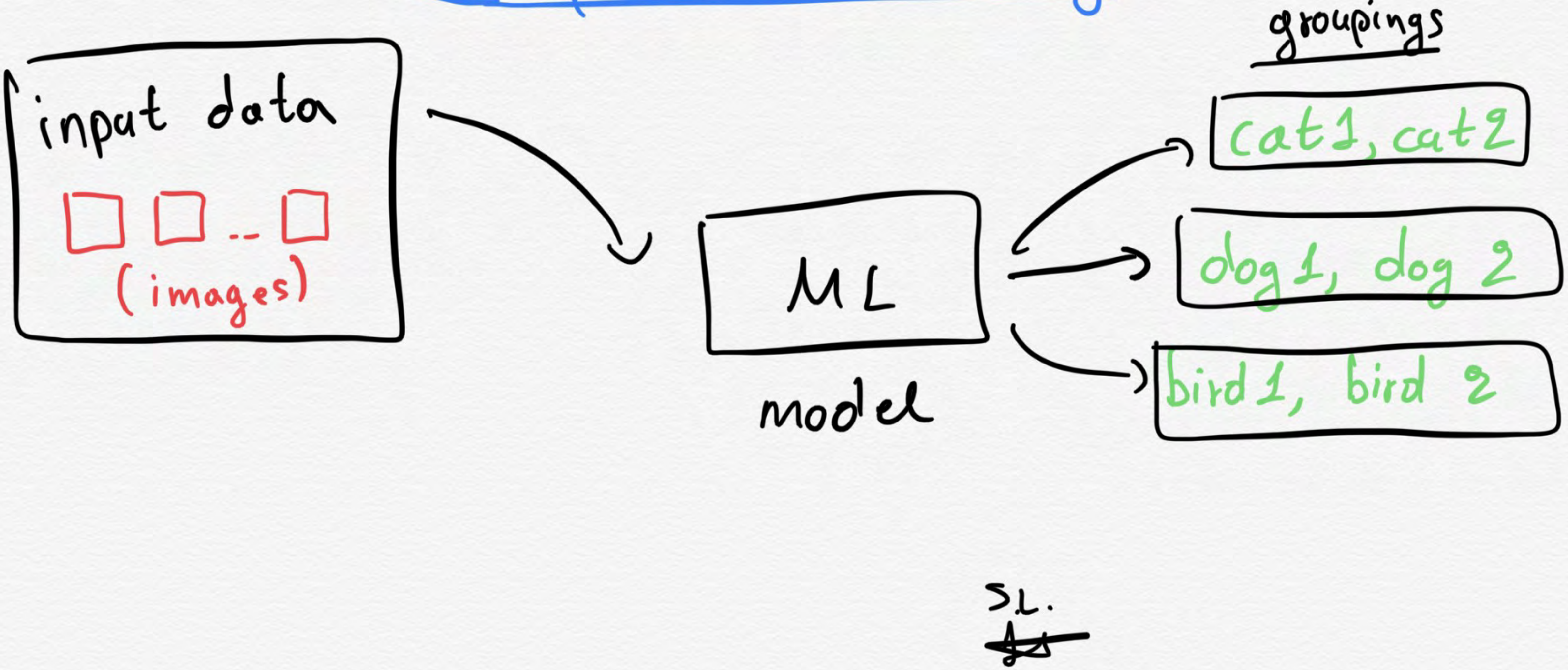
Some dataset observations are labeled
Most are usually unlabeled.
A mixture of supervised and unsupervised methods are used

Supervised learning



S.L.

Unsupervised learning



DOGS	CATS


a
b
c
d
e
f
g

Cat that looks like a dog

THANK YOU

Digital | Artificial Intelligence | Machine Learning

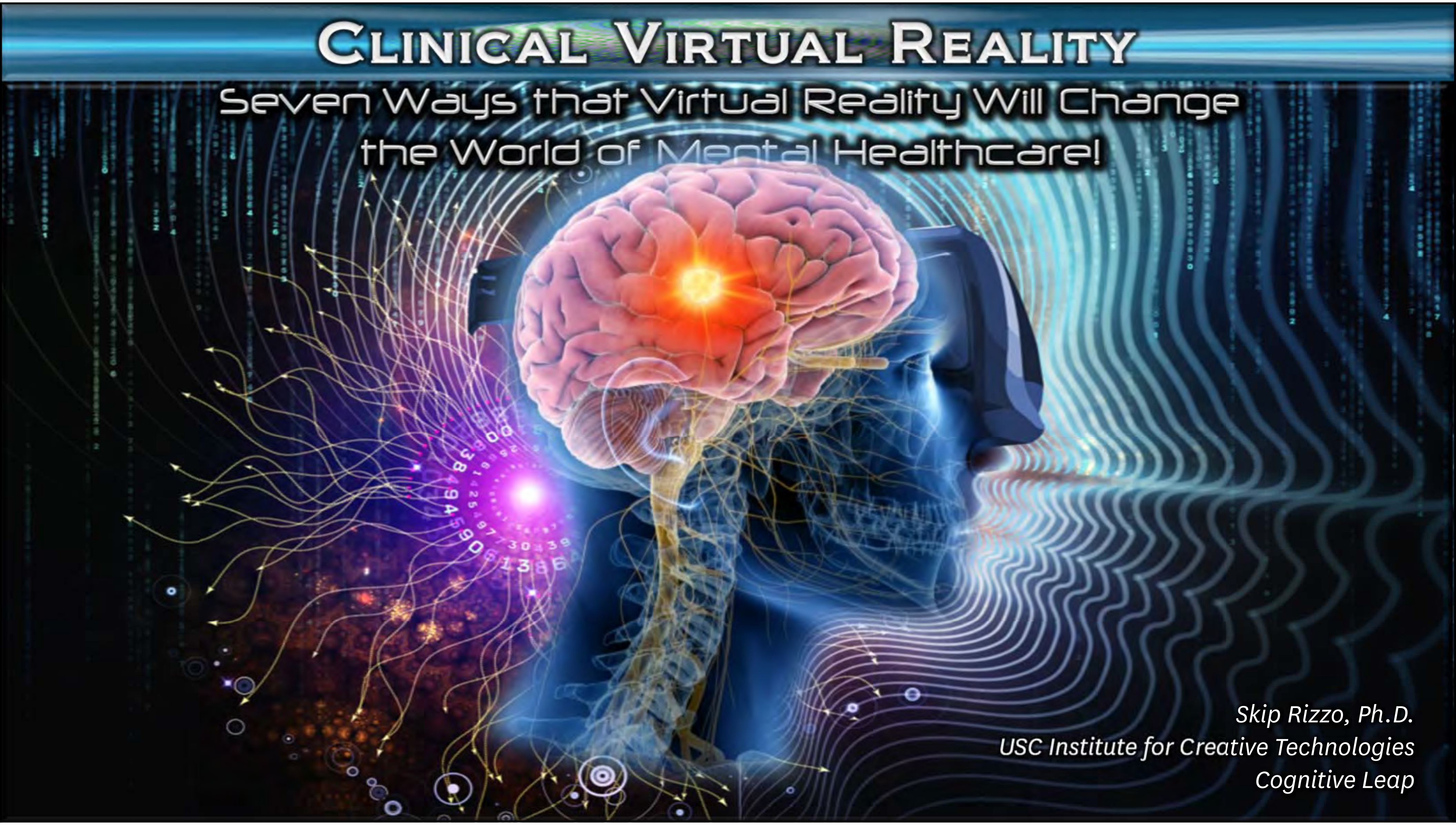
What are they, and *How* are they used

27 AUG 2021

Steve Thompson, Director Industry Solutions

Steven.Thompson@valgenesis.com

Mobile
(01) 805-509-4012


CLINICAL VIRTUAL REALITY
Seven Ways that Virtual Reality Will Change
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Skip Rizzo, Ph.D.
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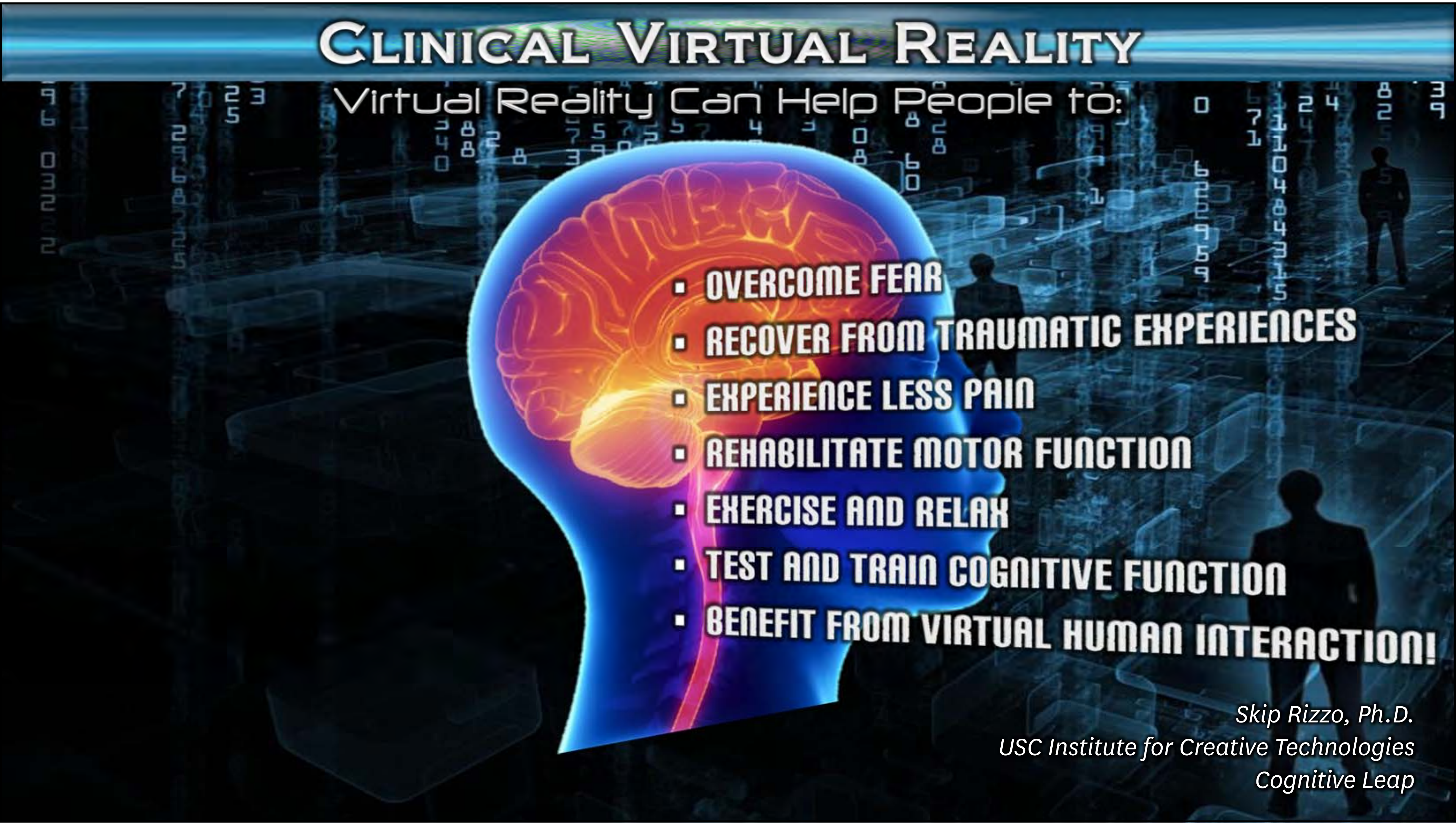
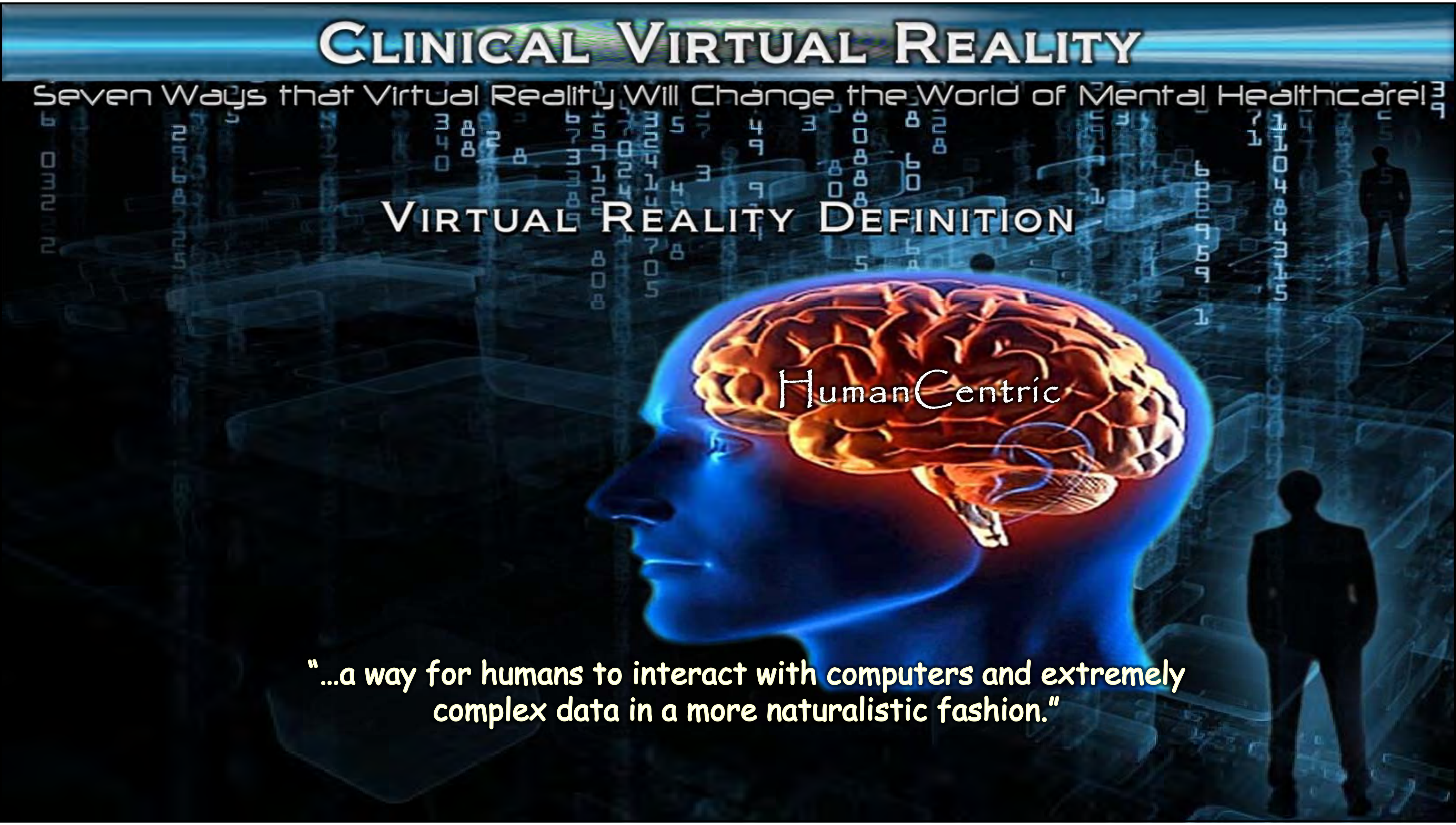
Cognitive Leap


CLINICAL VIRTUAL REALITY
Virtual Reality Can Help People to:
OVERCOME FEAR
RECOVER FROM TRAUMATIC EXPERIENCES
EXPERIENCE LESS PAIN
REHABILITATE MOTOR FUNCTION
EXERCISE AND RELAX
TEST AND TRAIN COGNITIVE FUNCTION
BENEFIT FROM VIRTUAL HUMAN INTERACTION!
Skip Rizzo, Ph.D.
USC Institute for Creative Technologies
Cognitive Leap


USC Institute for
Creative Technologies


VR EXPOSURE THERAPY & RESILIENCE TRAINING
Assessment
SCORE 0
98 MILES TO GO!
GO!
Promoting Access
Game-Based Rehab
Cerebral Palsy Family Forum


CLINICAL VIRTUAL REALITY
Seven Ways that Virtual Reality Will Change the World of Mental Healthcare!
VIRTUAL REALITY DEFINITION
TECHNOCENTRIC
VR integrates realtime computer processing, interface technology, body tracking & sensory displays to support a user to interact with and/or become immersed in a computer generated simulated environment.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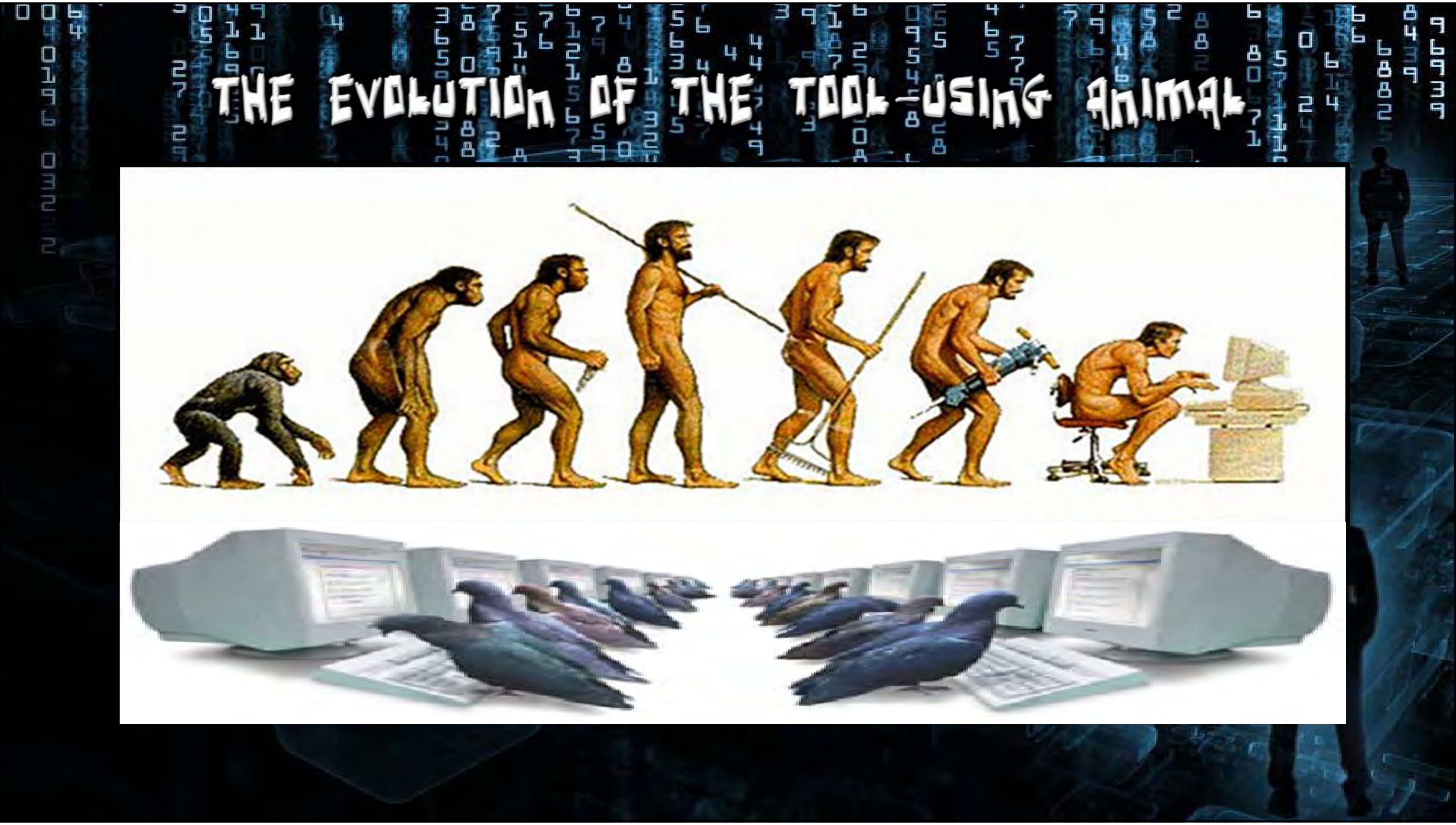
VIRTUAL REALITY DEFINITION
HumanCentric
"...a way for humans to interact with computers and extremely complex data in a more naturalistic fashion."


THE EVOLUTION OF THE TOOL-USING ANIMAL

Virtual Reality as a Simulation Technology

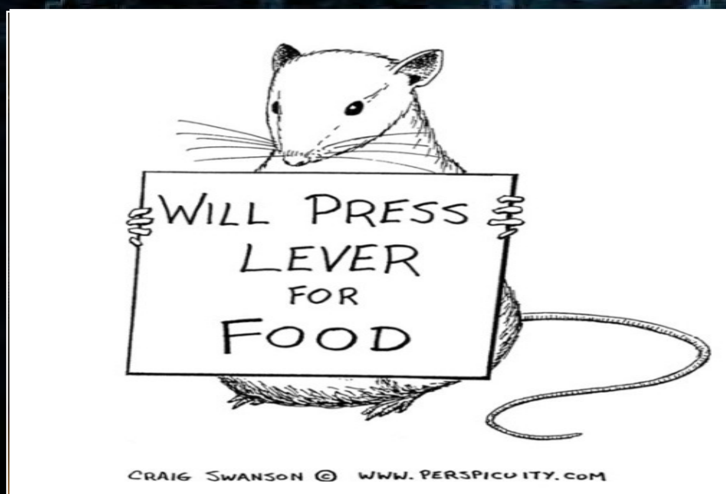
=

1st Link Aviation Simulator (1929)

Virtual Reality (2022)

To Test and Train
Piloting Ability

To Test, Train, Teach & Treat
Psychological, Cognitive, & Motor Functioning



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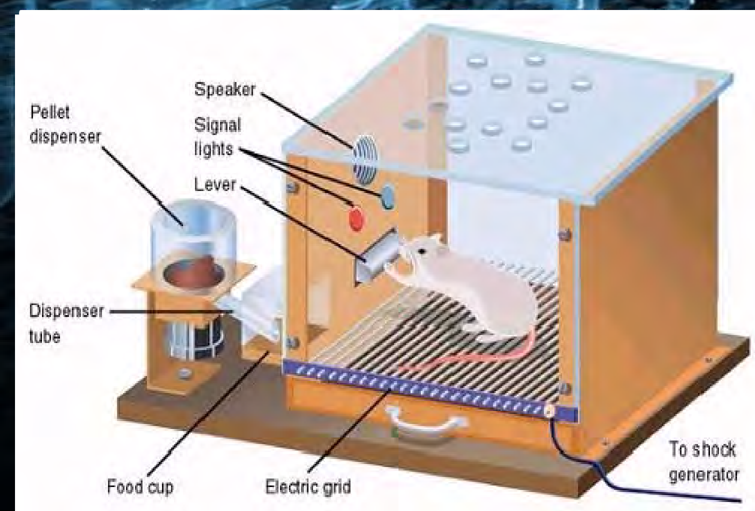
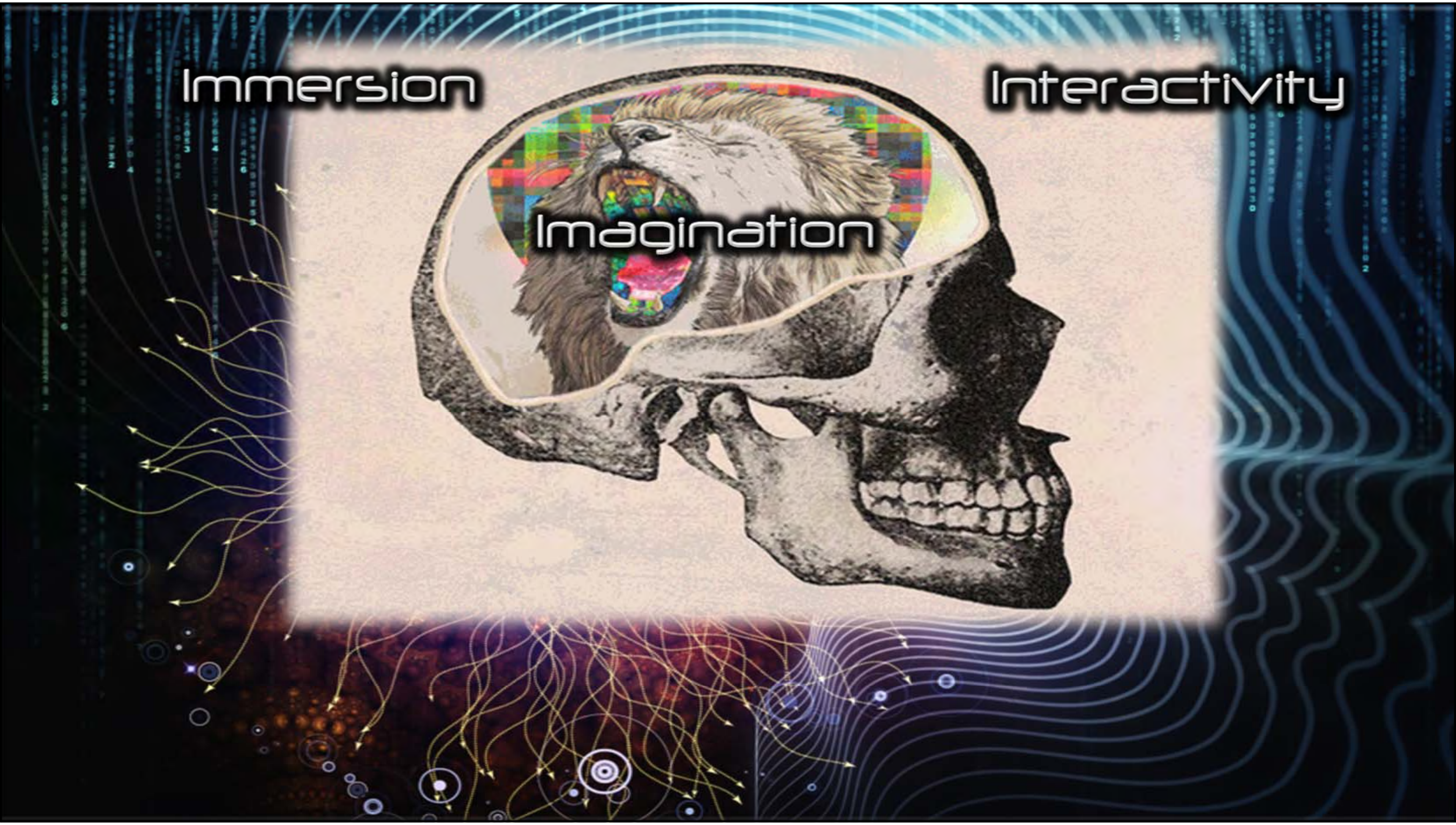


1st Link Aviation Simulator (1929)

Virtual Reality (2022)

THE ULTIMATE SKINNER BOX


Immersion
Interactivity
Imagination

Immersion

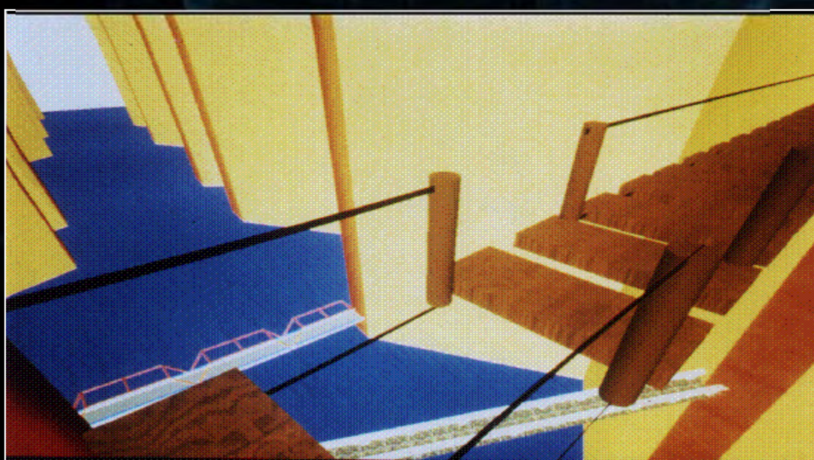
Immersion


Interactivity
DAN MARINO
FOUNDATION
Cranky Interviewer!
Job Interview Trainer for High
Functioning Autism Spectrum Disorder

A Revolution in Clinical VR Application R&D

1994

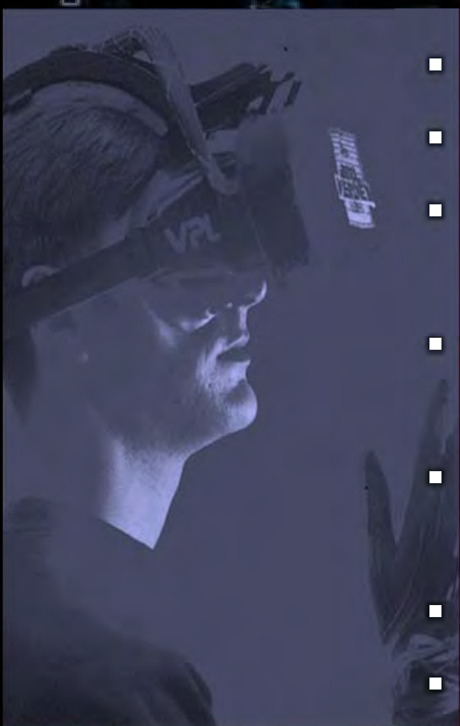
From Specific Phobias to



2022

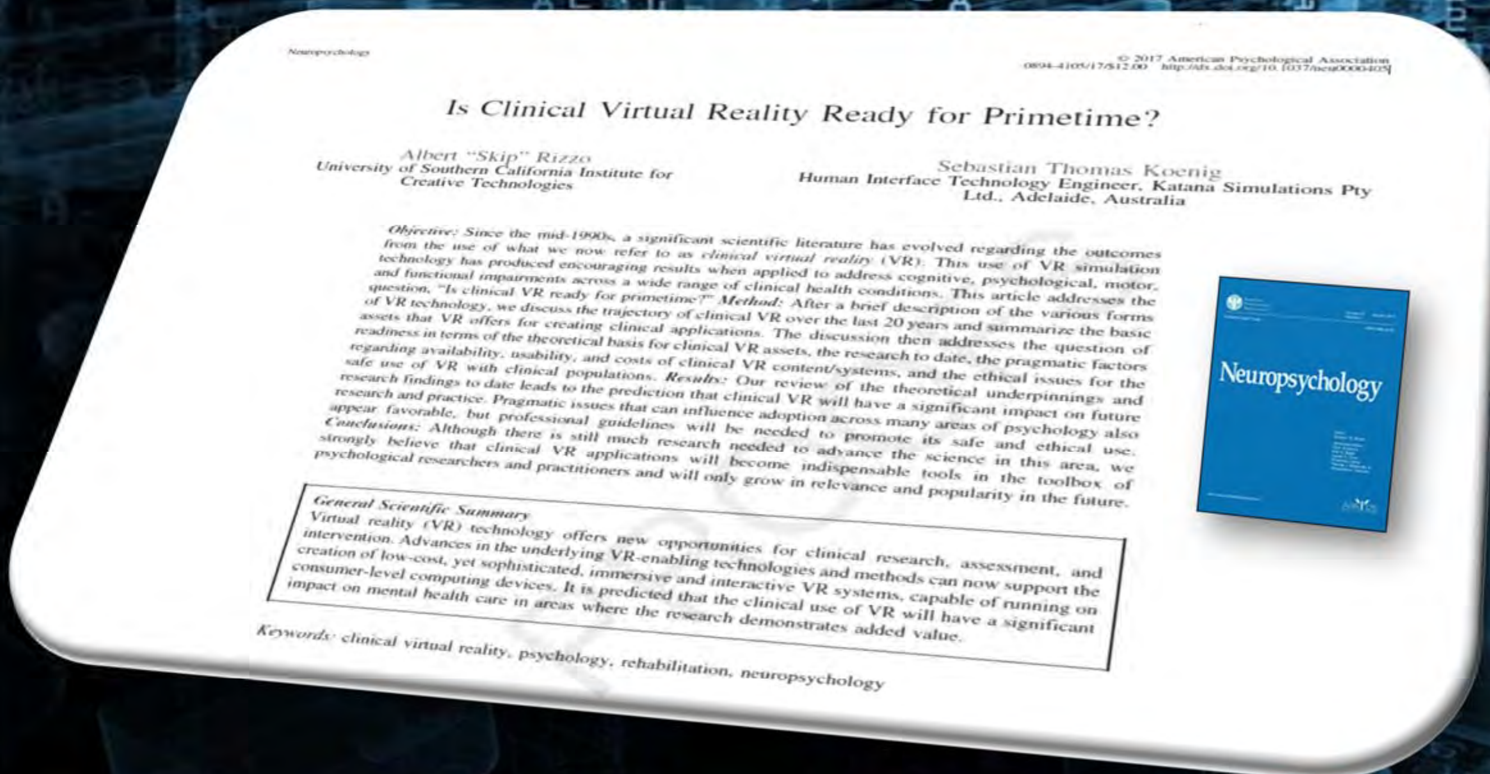
- PTSD
- Addiction
- Persecutory Delusions
- Depression
- Acute Pain Distraction
- Chronic Pain
- Autism
- ADHD
- Stroke, TBI, Parkinson's
- Spinal Cord Injury
- Cerebral Palsy
- Enhancing Empathy
- And Many More...

Virtual Reality Assets



- Ecological validity
- Stimulus control and consistency
- Repetitive and hierarchical stimulus delivery possible
- Self-guided exploration and independent practice
- Stimulus and response modification contingent on user's impairments
- Complete naturalistic performance record
- Cueing stimuli for "errorless learning"
- Real time performance feedback
- Safe testing and training environment which minimizes risks due to errors
- Graduated, systematic exposure
- Distraction Control
- Gaming factors to enhance motivation
- Low cost functional environments that can be duplicated and distributed
- Patient ENGAGEMENT!!!

Virtual Reality Assets



Neuropsychology

© 2017 American Psychological Association
0894-4105/17/$12.00 http://dx.doi.org/10.1037/neu0000405

Is Clinical Virtual Reality Ready for Primetime?

Albert "Skip" Rizzo
University of Southern California Institute for Creative Technologies

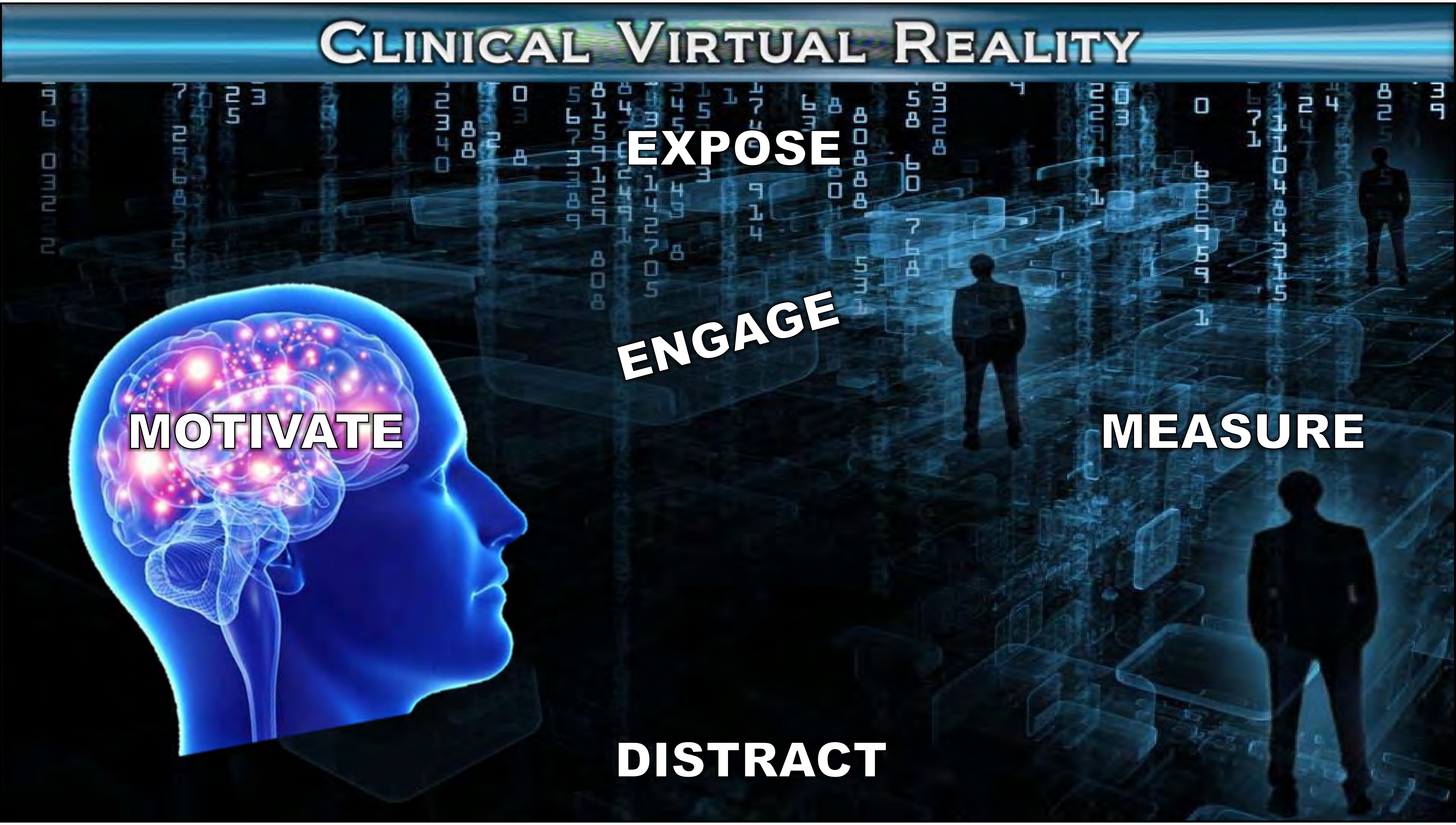
Sebastian Thomas Koenig
Human Interface Technology Engineer, Katana Simulations Pty Ltd., Adelaide, Australia

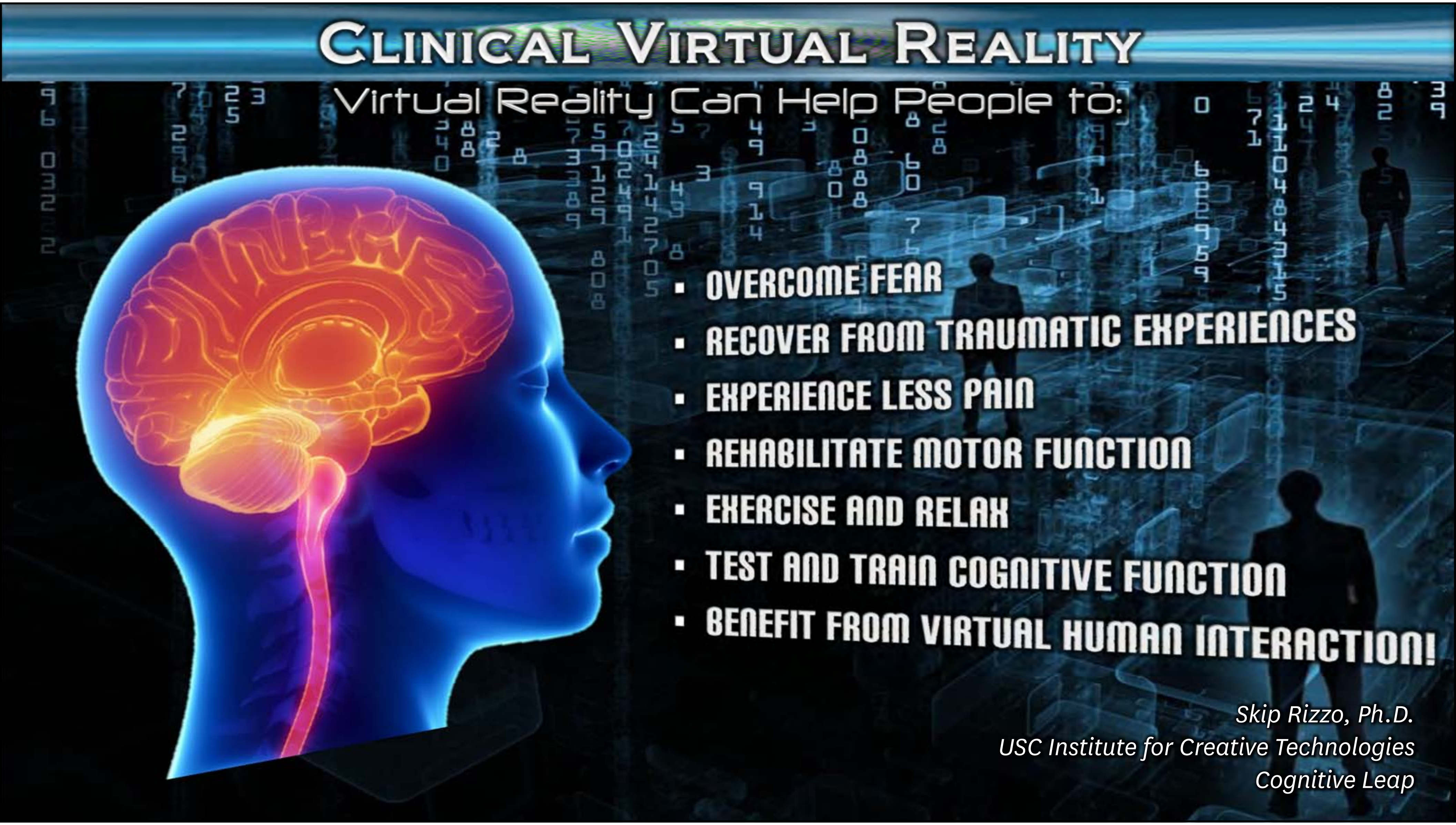
Objective: Since the mid-1990s, a significant scientific literature has evolved regarding the outcomes from the use of what we now refer to as *clinical virtual reality* (VR). This use of VR simulation technology has produced encouraging results when applied to address cognitive, psychological, motor, 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:*** Although 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.

General Scientific Summary
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 health care in areas where the research demonstrates added value.

Keywords: clinical virtual reality, psychology, rehabilitation, neuropsychology

APA Journal: Neuropsychology, Dec. 2017


CLINICAL VIRTUAL REALITY
EXPOSE
ENGAGE
MOTIVATE
MEASURE
DISTRACT

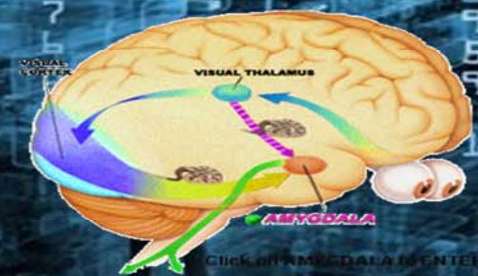

CLINICAL VIRTUAL REALITY
Virtual Reality Can Help People to:
OVERCOME FEAR
RECOVER FROM TRAUMATIC EXPERIENCES
EXPERIENCE LESS PAIN
REHABILITATE MOTOR FUNCTION
EXERCISE AND RELAX
TEST AND TRAIN COGNITIVE FUNCTION
BENEFIT FROM VIRTUAL HUMAN INTERACTION!
Skip Rizzo, Ph.D.
USC Institute for Creative Technologies
Cognitive Leap


1. Overcome Fear

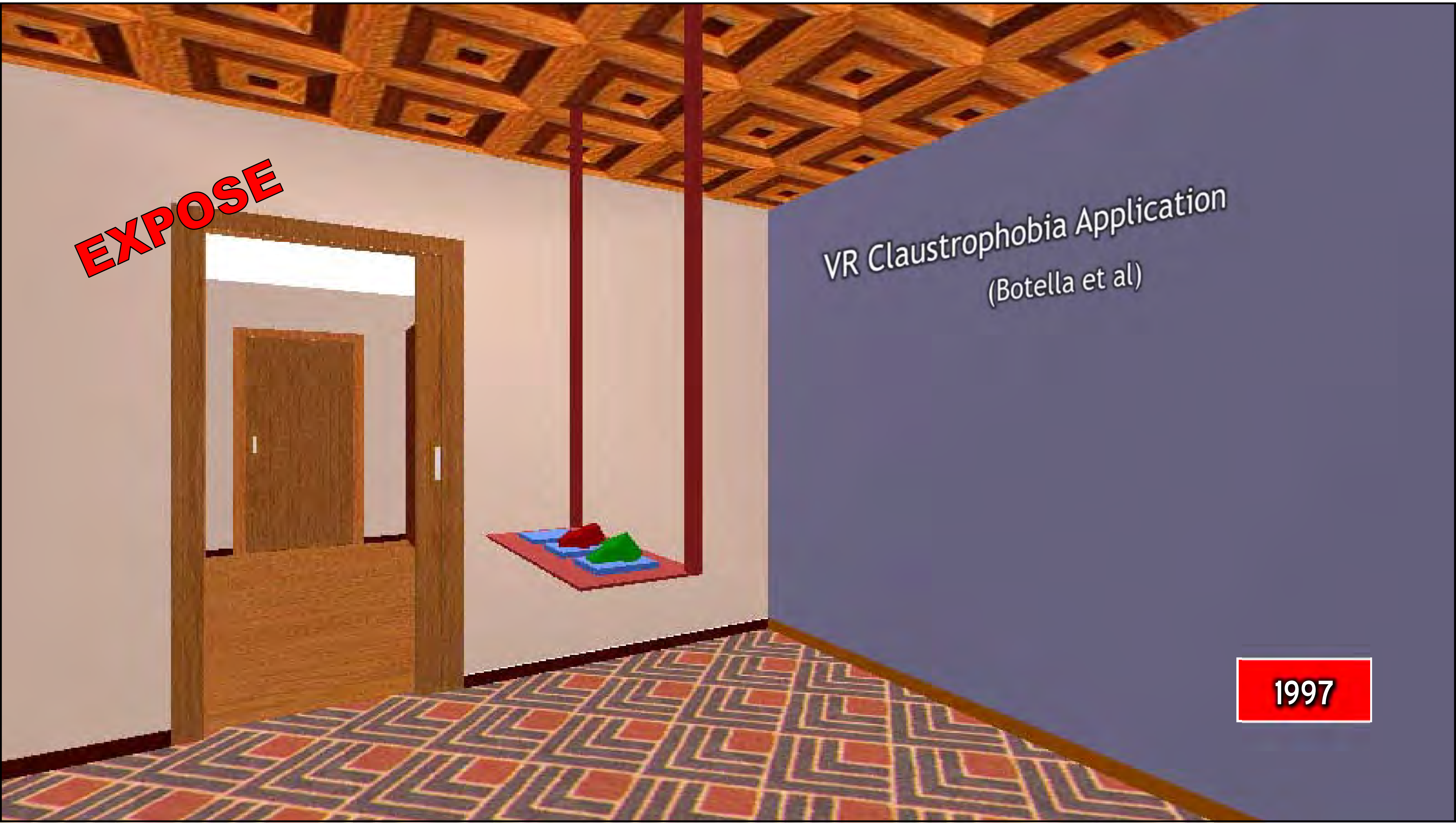
In the beginning. . .

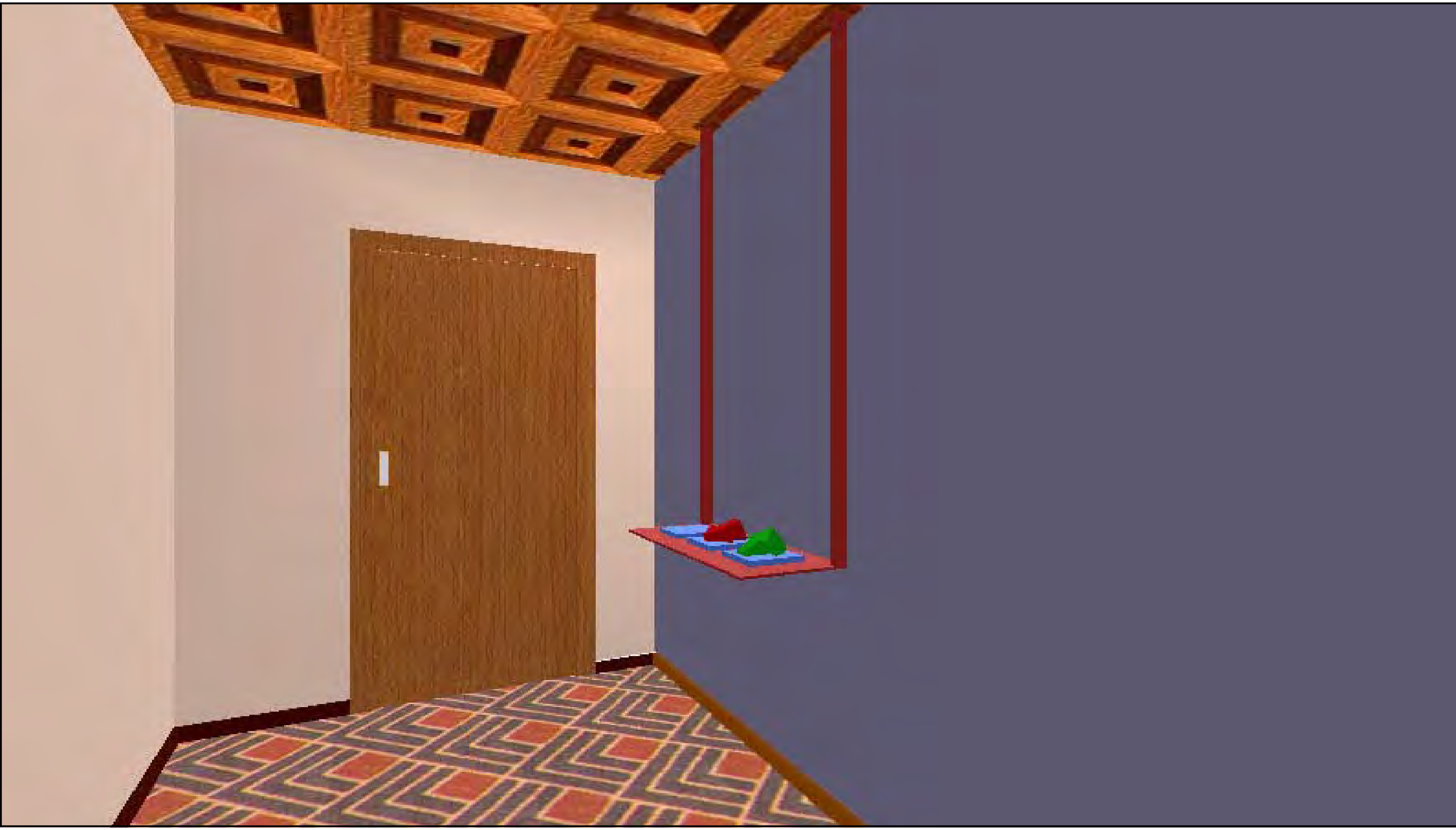
Exposure Therapy!

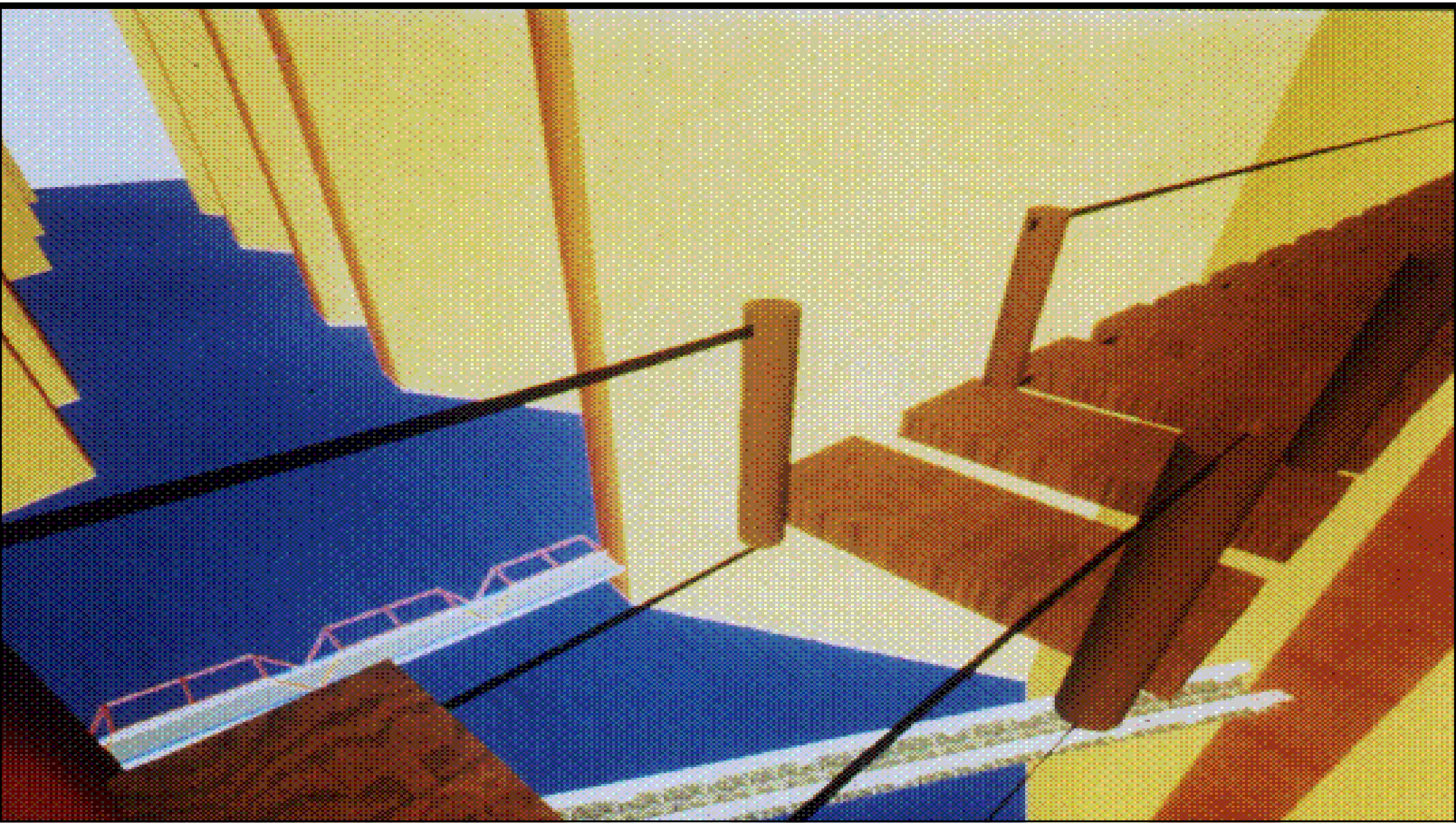
Theoretical Basis: *Exposure Therapy for Anxiety Disorders and PTSD*



The aim of exposure is to help the patient to confront the feared stimulus in order to correct the dysfunctional associations that have been established between the stimulus and perceived threat (e.g, it is dangerous, I can't cope).


EXPOSE
VR Claustrophobia Application
(Botella et al)
1997





Fear of Heights 2017
Samsung
Befearless - Heights
EXPOSE
Samsung VR Headsets Help Millennials Overcome Their Fears in Persuasive New Ads
Train your phobias away with realistic simulations
By Gabriel Beltrone


Fear of Public Speaking
Fear of Heights
Fear of Crowds
Fear of Flying


PHOBIAS DIFFER FROM "NORMAL" FEAR OF OBJECTIVE THREAT...
15 Planes would have to fall out of the sky each day
to match the number of automobile-related deaths...
FEAR OF FLYING

VR Anxiety Disorders Meta-Analyses

EXPOSE

ELSEVIER

Journal of Anxiety Disorders 22 (2008) 561–569

Anxiety Disorders

Review

Virtual reality exposure therapy for anxiety disorders: A meta-analysis

Mark B. Powers *, Paul M.G. Emmelkamp

University of Amsterdam, The Netherlands

Received 1 March 2007; received in revised form 11 April 2007; accepted 20 April 2007

Abstract

There is now a substantial literature investigating virtual reality exposure therapy (VRET) as a viable treatment option for anxiety disorders. In this meta-analysis we provide effect size estimates for virtual reality treatment in comparison to in vivo exposure and control conditions (waitlist, attention control, etc.). A comprehensive search of the literature identified 13 studies ($n = 397$) that were included in the final analyses. Consistent with prediction the primary random effects analysis showed a large mean effect size for VRET compared to control conditions, Cohen's $d = 1.11$ (S.E. = 0.15, 95% CI: 0.82–1.39). This finding was consistent across secondary outcome categories as well (domain-specific, general subjective distress, cognition, behavior, and psychophysiology). Also as expected in vivo treatment was not significantly more effective than VRET. In fact, there was a small effect size favoring VRET over in vivo conditions, Cohen's $d = 0.35$ (S.E. = 0.15, 95% CI: 0.05–0.65). There was a trend for a dose-response relationship with more VRET sessions showing larger effects ($p = 0.06$). Outcome was not related to publication year or sample size. Implications are discussed.

Keywords: Virtual reality; Exposure therapy; Anxiety disorders; Meta-analysis

Journal of Anxiety Disorders

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

Journal of Behavior Therapy and Experimental Psychiatry ■ (■■■■) ■■■–■■■

JOURNAL OF behavior therapy and experimental psychiatry

www.elsevier.com/locate/jbtep

Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis

Thomas D. Parsons*, Albert A. Rizzo

Institute for Creative Technologies, University of Southern California, 13274 Fiji Way, Office 301, Marina del Rey, CA 90292-4019, USA

Received 24 October 2006; received in revised form 6 July 2007; accepted 18 July 2007

Abstract

Virtual reality exposure therapy (VRET) is an increasingly common treatment for anxiety and specific phobias. Lacking is a quantitative meta-analysis that enhances understanding of the variability and clinical significance of anxiety reduction outcomes after VRET. Searches of electronic databases yielded 52 studies, and of these, 21 studies (300 subjects) met inclusion criteria. Although meta-analysis revealed large declines in anxiety symptoms following VRET, moderator analyses were limited due to inconsistent reporting in the VRET literature. This highlights the need for future research studies that report uniform and detailed information regarding presence, immersion, anxiety and/or phobia duration, and demographics.

Keywords: Virt ... roscience

Journal of Behavior Therapy and Experimental Psychiatry

2008

Behaviour Research and Therapy 74 (2015) 18–24

Contents lists available at ScienceDirect

Behaviour Research and Therapy

journal homepage: www.elsevier.com/locate/brat

Can virtual reality exposure therapy gains be generalized to real-life? A meta-analysis of studies applying behavioral assessments

Nexhmedin Morina [a, b, *], Hiske Ijntema [a], Katharina Meyerbröker [c], Paul M.G. Emmelkamp [d, e]

[a] Department of Clinical Psychology, University of Amsterdam, Amsterdam, The Netherlands
[b] Amsterdam Brain and Cognition Center, University of Amsterdam, Amsterdam, The Netherlands
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[d] Netherlands Institute for Advanced Study, Wassenaar, The Netherlands
[e] Center for Social and Humanities Research, King AbdulAziz University, Jeddah, Saudi Arabia

ARTICLE INFO

Article history:
Received 12 November 2014
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7 August 2015
Accepted 27 August 2015
Available online 31 August 2015

Keywords:
Virtual reality therapy
Behavioral assessment
Specific phobias
Anxiety disorders
Meta-analysis

ABSTRACT

In virtual reality exposure therapy (VRET), patients are exposed to virtual environments that resemble feared real-life situations. The aim of the current study was to assess the extent to which VRET gains can be observed in real-life situations. We conducted a meta-analysis of clinical trials applying VRET to specific phobias and measuring treatment outcome by means of behavioral laboratory tests or recordings of behavioral activities in real-life. Data sources were searches of databases (Medline, PsycInfo, and Cochrane). We included in total 14 clinical trials on specific phobias. Results revealed that patients undergoing VRET did significantly better on behavioral assessments following treatment than before treatment, with an aggregated uncontrolled effect size of g = 1.23. Furthermore, patients undergoing VRET performed better on behavioral assessments at post-treatment than patients on wait-list (g = 1.41). Additionally, results of behavioral assessments at post-treatment and at follow-up revealed no significant differences between VRET and exposure in vivo (g = −0.09 and 0.53, respectively). Finally, behavioral measurement effect sizes were similar to those calculated from self-report measures. The findings demonstrate that VRET can produce significant behavior change in real-life situations and support its application in treating specific phobias.

VR Anxiety Disorders Meta-Analyses

EXPOSE

Behaviour Research and Therapy 74 (2015) 18–24

Contents lists available at ScienceDirect

Behaviour Research and Therapy

journal homepage: www.elsevier.com/locate/brat

ELSEVIER

BEHAVIOUR RESEARCH AND THERAPY

CrossMark

Can virtual reality exposure therapy gains be generalized to real-life? A meta-analysis of studies applying behavioral assessments

Nexhmedin Morina [a, b, *], Hiske Ijntema [a], Katharina Meyerbröker [c], Paul M.G. Emmelkamp [d, e]

[a] Department of Clinical Psychology, University of Amsterdam, Amsterdam, The Netherlands
[b] Amsterdam Brain and Cognition Center, University of Amsterdam, Amsterdam, The Netherlands
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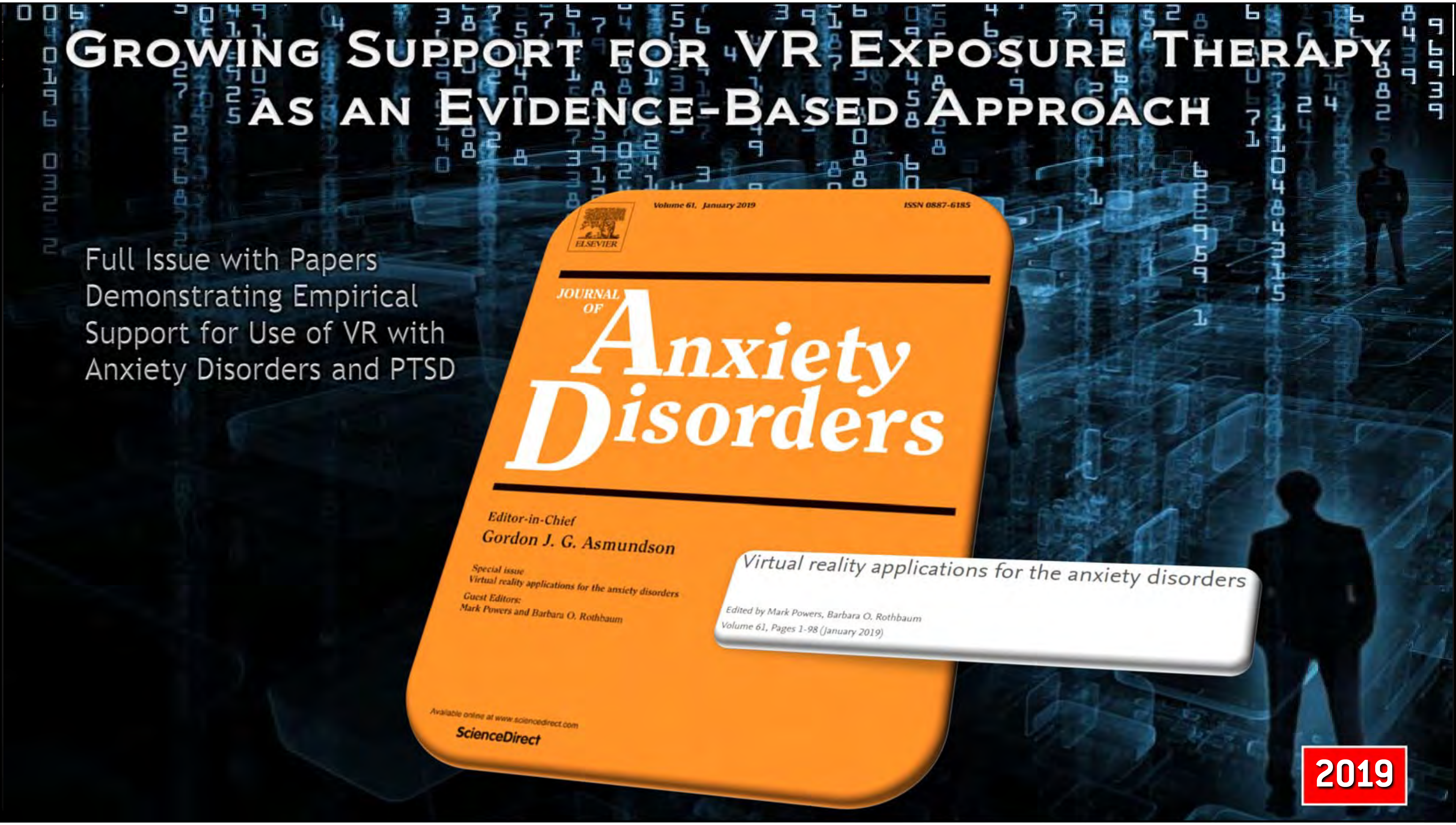
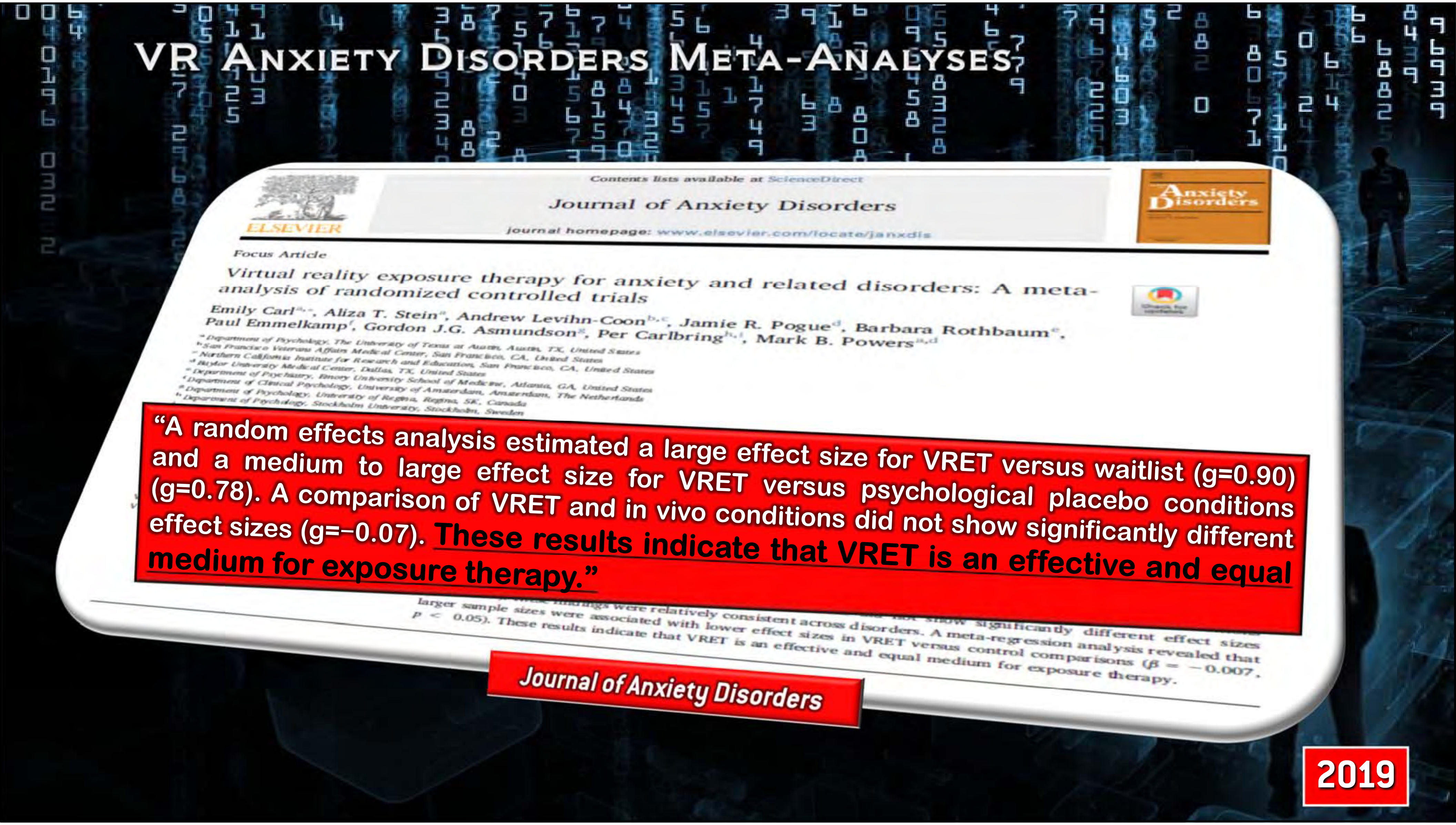
Behaviour Research and Therapy

2015


GROWING SUPPORT FOR VR EXPOSURE THERAPY AS AN EVIDENCE-BASED APPROACH
Full Issue with Papers Demonstrating Empirical Support for Use of VR with Anxiety Disorders and PTSD
Volume 61, January 2019
ISSN 0887-6185
ELSEVIER
JOURNAL OF Anxiety Disorders
Editor-in-Chief
Gordon J. G. Asmundson
Special issue
Virtual reality applications for the anxiety disorders
Guest Editors:
Mark Powers and Barbara O. Rothbaum
Available online at www.sciencedirect.com
ScienceDirect
Virtual reality applications for the anxiety disorders
Edited by Mark Powers, Barbara O. Rothbaum
Volume 61, Pages 1-98 (January 2019)
2019


VR Anxiety Disorders Meta-Analyses
Contents lists available at ScienceDirect
Journal of Anxiety Disorders
journal homepage: www.elsevier.com/locate/janxdis
ELSEVIER
Anxiety Disorders
Focus Article
Virtual reality exposure therapy for anxiety and related disorders: A meta-analysis of randomized controlled trials
Emily Carl, Aliza T. Stein, Andrew Levihn-Coon, Jamie R. Pogue, Barbara Rothbaum, Paul Emmelkamp, Gordon J.G. Asmundson, Per Carlbring, Mark B. Powers
"A random effects analysis estimated a large effect size for VRET versus waitlist (g=0.90) and a medium to large effect size for VRET versus psychological placebo conditions (g=0.78). A comparison of VRET and in vivo conditions did not show significantly different effect sizes (g=−0.07). These results indicate that VRET is an effective and equal medium for exposure therapy."
Journal of Anxiety Disorders
2019


2. Overcome Traumatic Experiences

Virtual Reality Exposure Therapy for Anxiety Disorders

- Heights
- Flying
- Driving
- Spiders/snakes
- Public Speaking
- Claustrophobia
- Generalized Social Phobia
- Panic Disorder w/Agoraphobia
- Posttraumatic Stress Disorder

VR PTSD Examples

- **Virtual Vietnam** – *Emory University (Rothbaum et al)*
- **World Trade Center** – *Weill Cornell Medical Center/U of Wash (Difede, Hoffman et al)*
- **Terrorist Bus Bombing** - *U. of Haifa/U of Wash (Josman et al)*
- **Motor Vehicle Accidents** – *Univ. of Buffalo (Beck et al)*
- **Emma's World** - *Universitat de València, Spain (Botella et al)*
- **Virtual Angola** – *U. of Lusófona de Humanidades e Tecnologias, Lisbon (Gamito et al)*
- Virtual Iraq/Afghanistan – *USC Institute for Creative Technologies (Rizzo , Hartholt, Pair et al)*

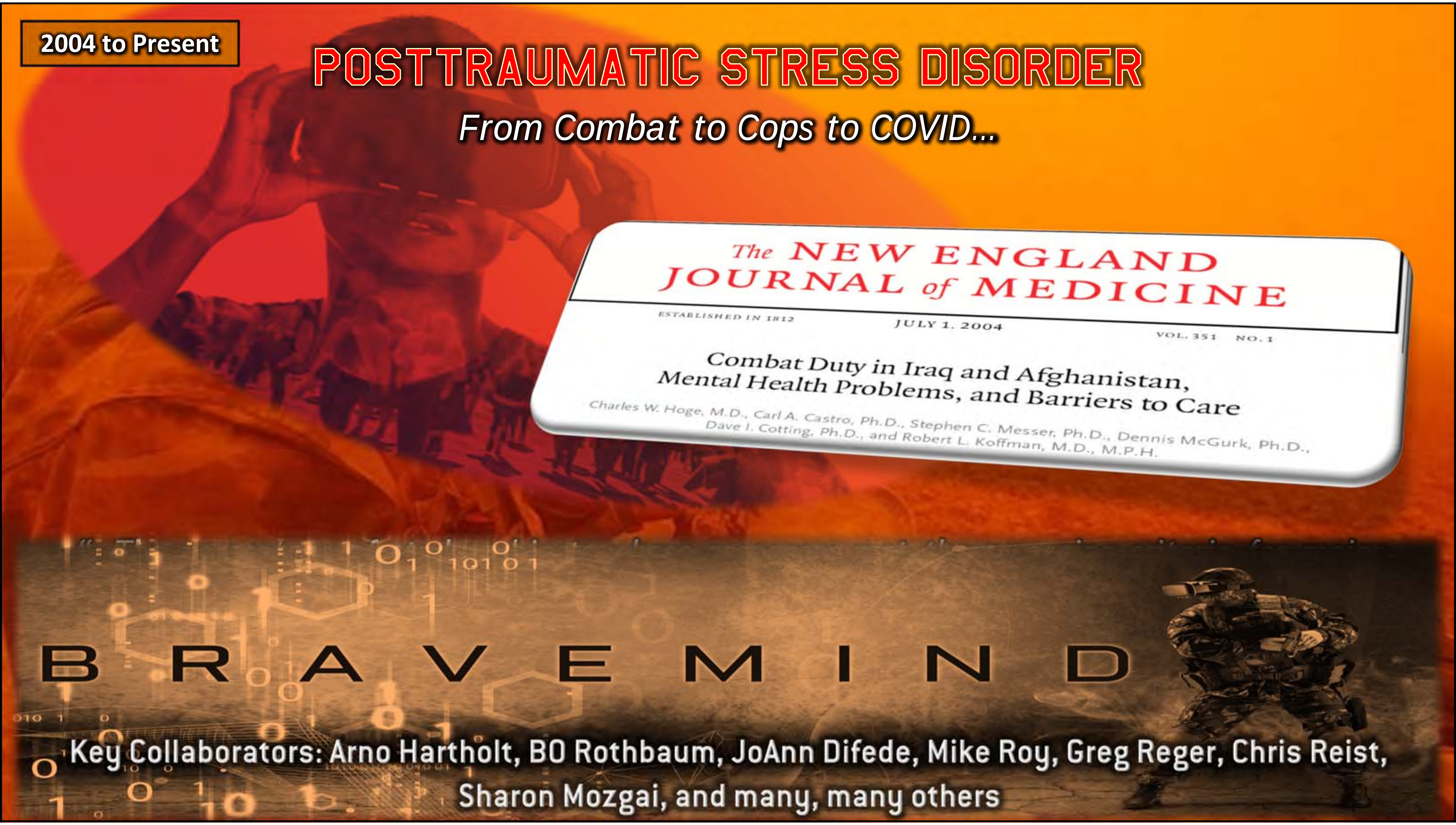
Posttraumatic Stress Disorder

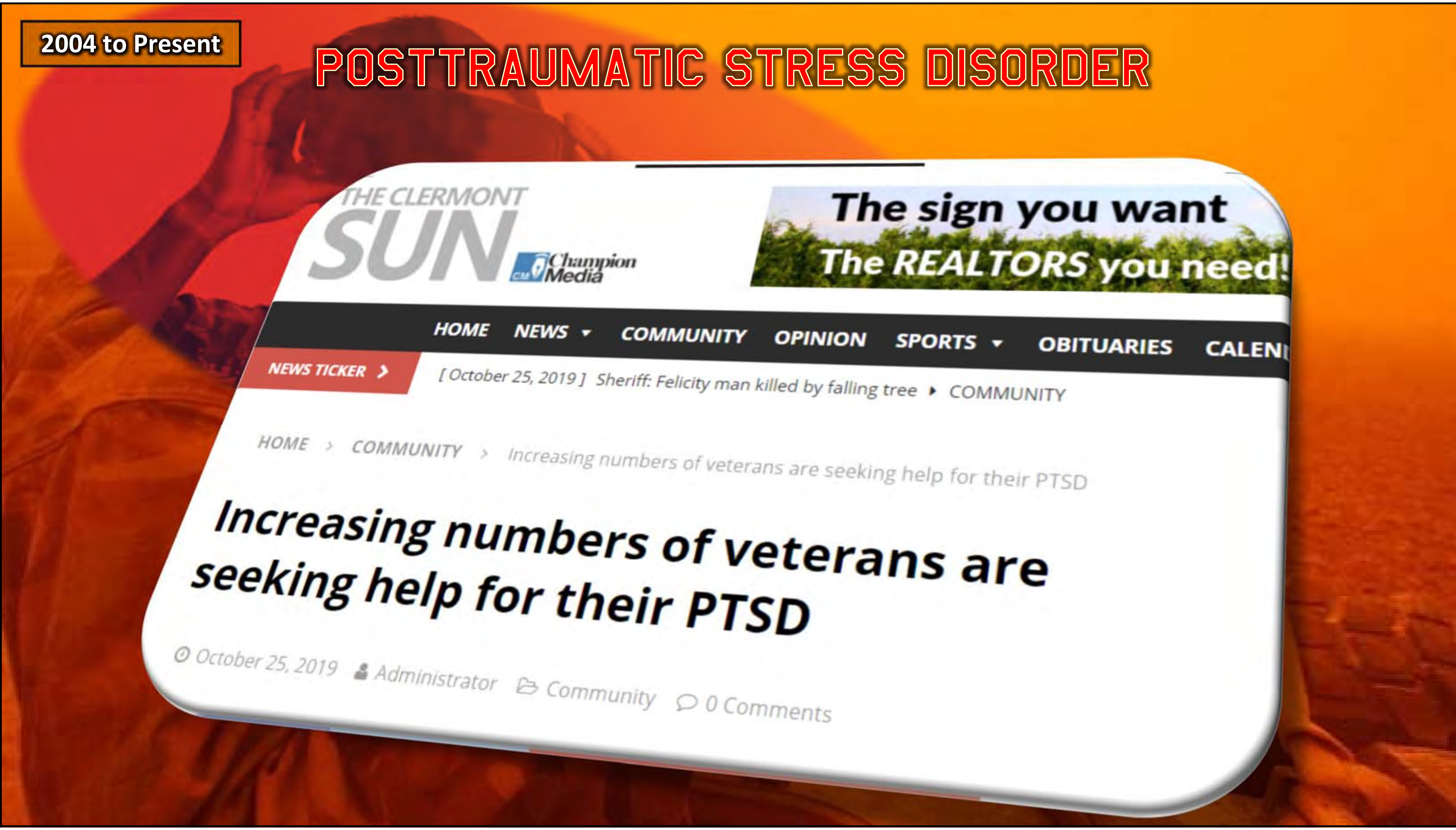
Why use Virtual Reality to Deliver Exposure Therapy?

"...some patients refuse to engage in the treatment, and others, though they express willingness, are unable to engage their emotions or senses."

(Difede & Hoffman, 2002)

Engagement Is Fundamental!


2004 to Present
POSTTRAUMATIC STRESS DISORDER
From Combat to Cops to COVID...
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812
JULY 1, 2004
VOL. 351 NO. 1
Combat Duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to Care
Charles W. Hoge, M.D., Carl A. Castro, Ph.D., Stephen C. Messer, Ph.D., Dennis McGurk, Ph.D., Dave I. Cotting, Ph.D., and Robert L. Koffman, M.D., M.P.H.
BRAVEMIND
Key Collaborators: Arno Hartholt, BO Rothbaum, JoAnn Difede, Mike Roy, Greg Reger, Chris Reist, Sharon Mozgai, and many, many others


2004 to Present
POSTTRAUMATIC STRESS DISORDER
THE CLERMONT SUN
Champion Media
The sign you want
The REALTORS you need!
HOME NEWS COMMUNITY OPINION SPORTS OBITUARIES CALEN
NEWS TICKER
[October 25, 2019] Sheriff: Felicity man killed by falling tree COMMUNITY
HOME > COMMUNITY > Increasing numbers of veterans are seeking help for their PTSD
Increasing numbers of veterans are seeking help for their PTSD
October 25, 2019 Administrator Community 0 Comments

CPT. GREG REGER PH.D.

98TH MED DET.

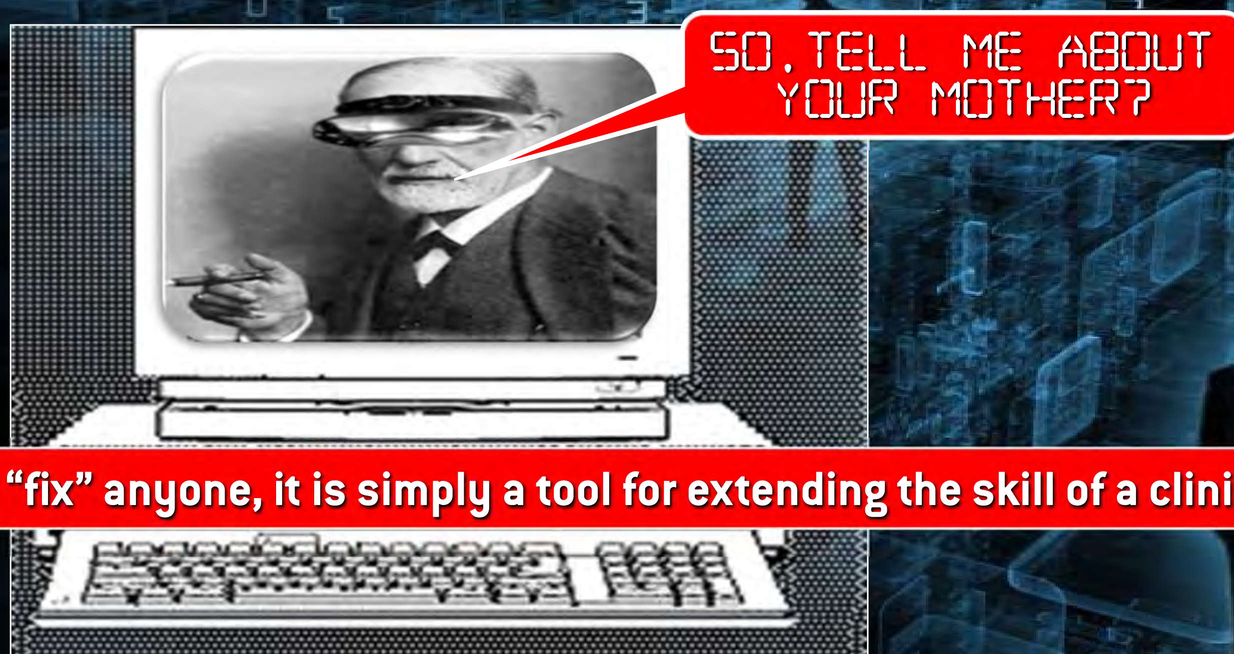
COMBAT STRESS CONTROL TEAM

TALLIL AB LSA ADDER IRAQ

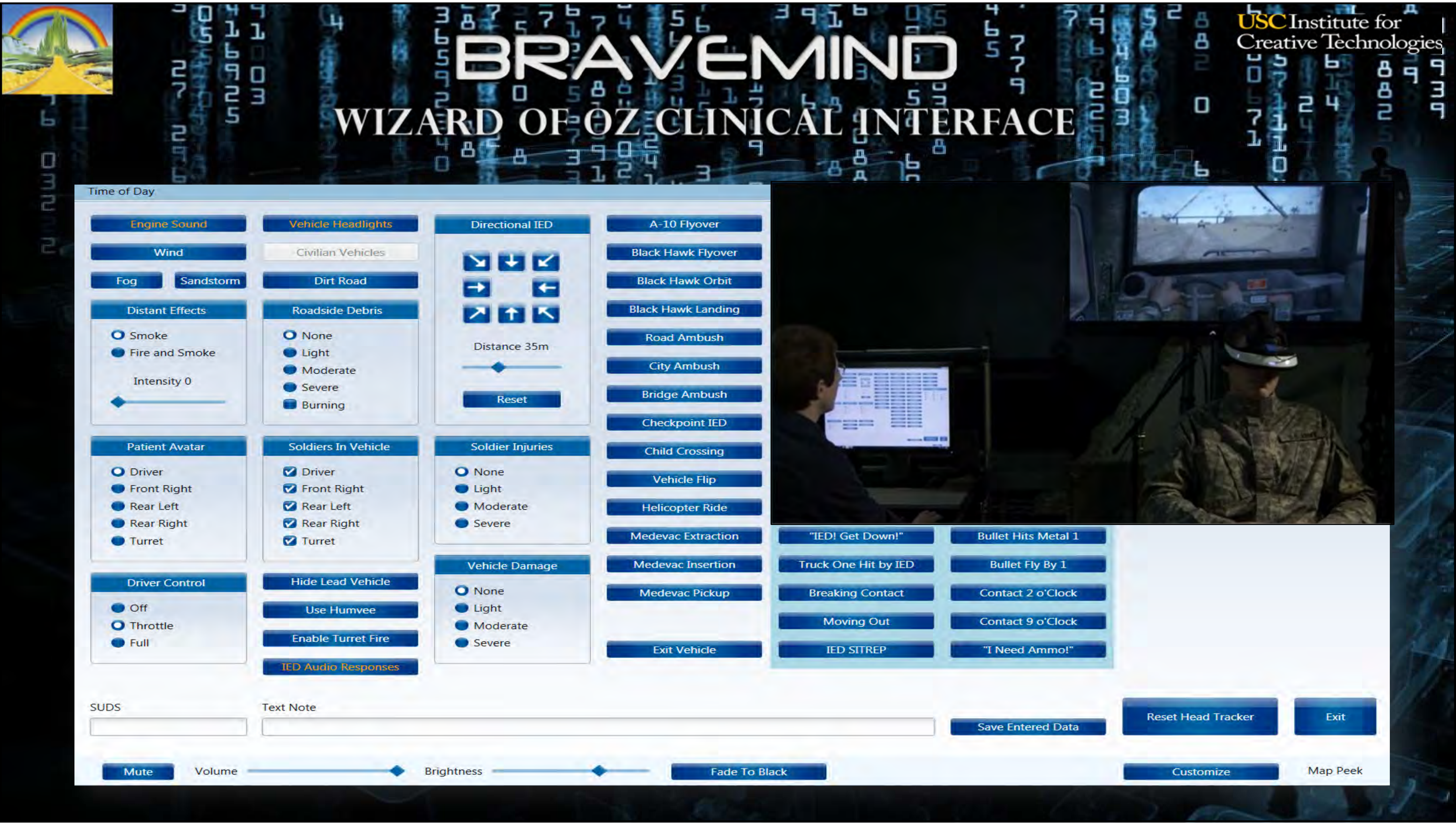
2004


2011-PRESENT
BRAVEMIND
PTS VIRTUAL REALITY EXPOSURE THERAPY
14 Diverse Customizable Sce
Treated as part of the Rothbaum study at Emory U

Need to Guard Against the perception that VR Tools are designed to eliminate the need for a Well Trained Clinician



Technology doesn't "fix" anyone, it is simply a tool for extending the skill of a clinician.


USC Institute for Creative Technologies
BRAVEMIND
WIZARD OF OZ CLINICAL INTERFACE
Time of Day
Engine Sound
Vehicle Headlights
Directional IED
A-10 Flyover
Wind
Civilian Vehicles
Black Hawk Flyover
Fog
Sandstorm
Dirt Road
Black Hawk Orbit
Distant Effects
Roadside Debris
Black Hawk Landing
Smoke
Fire and Smoke
Intensity 0
None
Light
Moderate
Severe
Burning
Distance 35m
Reset
Road Ambush
City Ambush
Bridge Ambush
Checkpoint IED
Patient Avatar
Driver
Front Right
Rear Left
Rear Right
Turret
Soldiers In Vehicle
Driver
Front Right
Rear Left
Rear Right
Turret
Soldier Injuries
None
Light
Moderate
Severe
Child Crossing
Vehicle Flip
Helicopter Ride
Medevac Extraction
"IED! Get Down!"
Bullet Hits Metal 1
Medevac Insertion
Truck One Hit by IED
Bullet Fly By 1
Medevac Pickup
Breaking Contact
Contact 2 o'Clock
Moving Out
Contact 9 o'Clock
Exit Vehicle
IED SITREP
"I Need Ammo!"
Driver Control
Off
Throttle
Full
Hide Lead Vehicle
Use Humvee
Enable Turret Fire
IED Audio Responses
Vehicle Damage
None
Light
Moderate
Severe
SUDS
Text Note
Save Entered Data
Reset Head Tracker
Exit
Mute
Volume
Brightness
Fade To Black
Customize
Map Peek

Natural Navigational Control

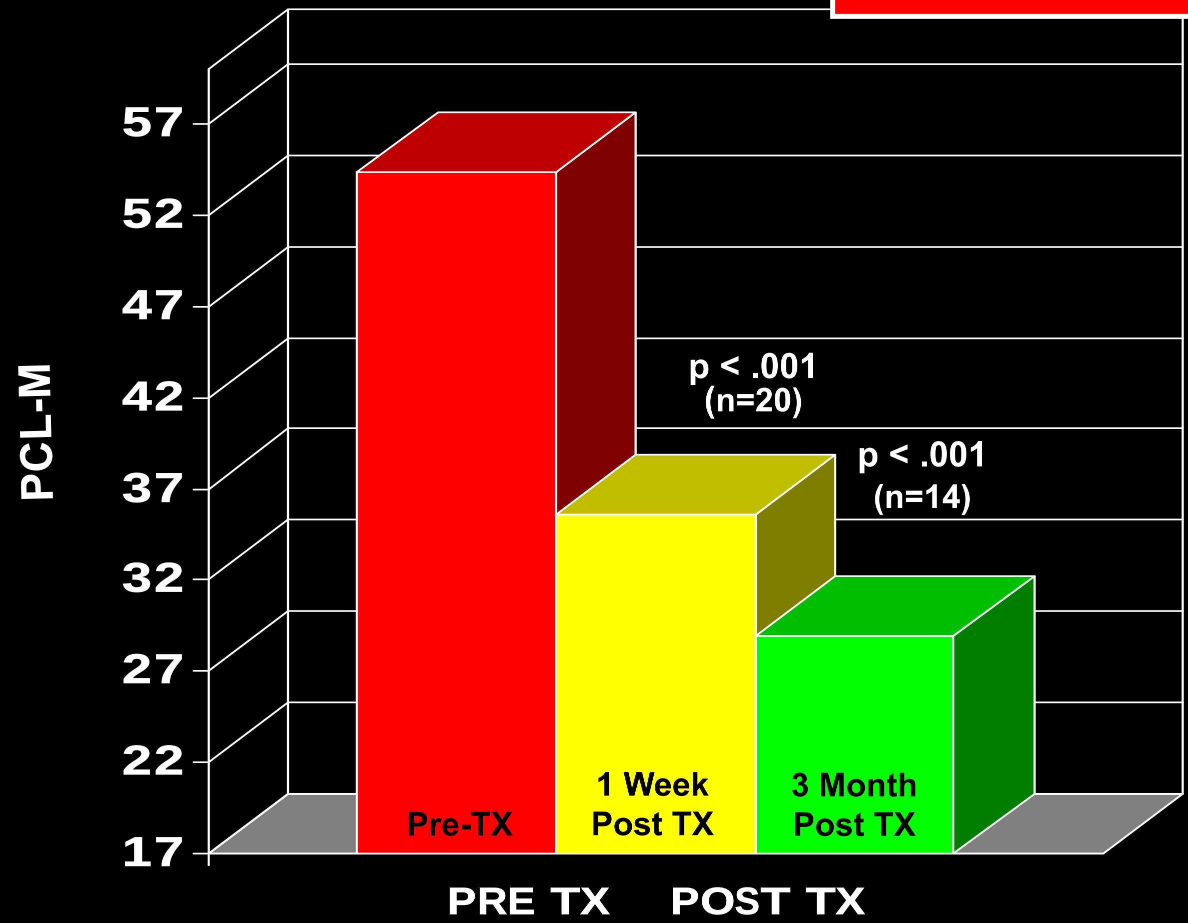

Clinical Research
DEPARTMENT OF THE NAVY
USN
ONR
Science & Technology
Skip Rizzo, Barbara Rothbaum, JoAnn Difede, Greg Reger CTR, Josh Spitalnick, Rob Mclay LCDR, Kevin Holloway, Judith Cukor Maryrose Gerardi, Mike Roy COL, Greg Gahm COL, & Russell Shilling CDR

Naval Med Center SD/Camp Pendleton

PTSD Checklist-Military (PCL-M)

PreTreatment, PostTreatment & 3 Month Follow-up

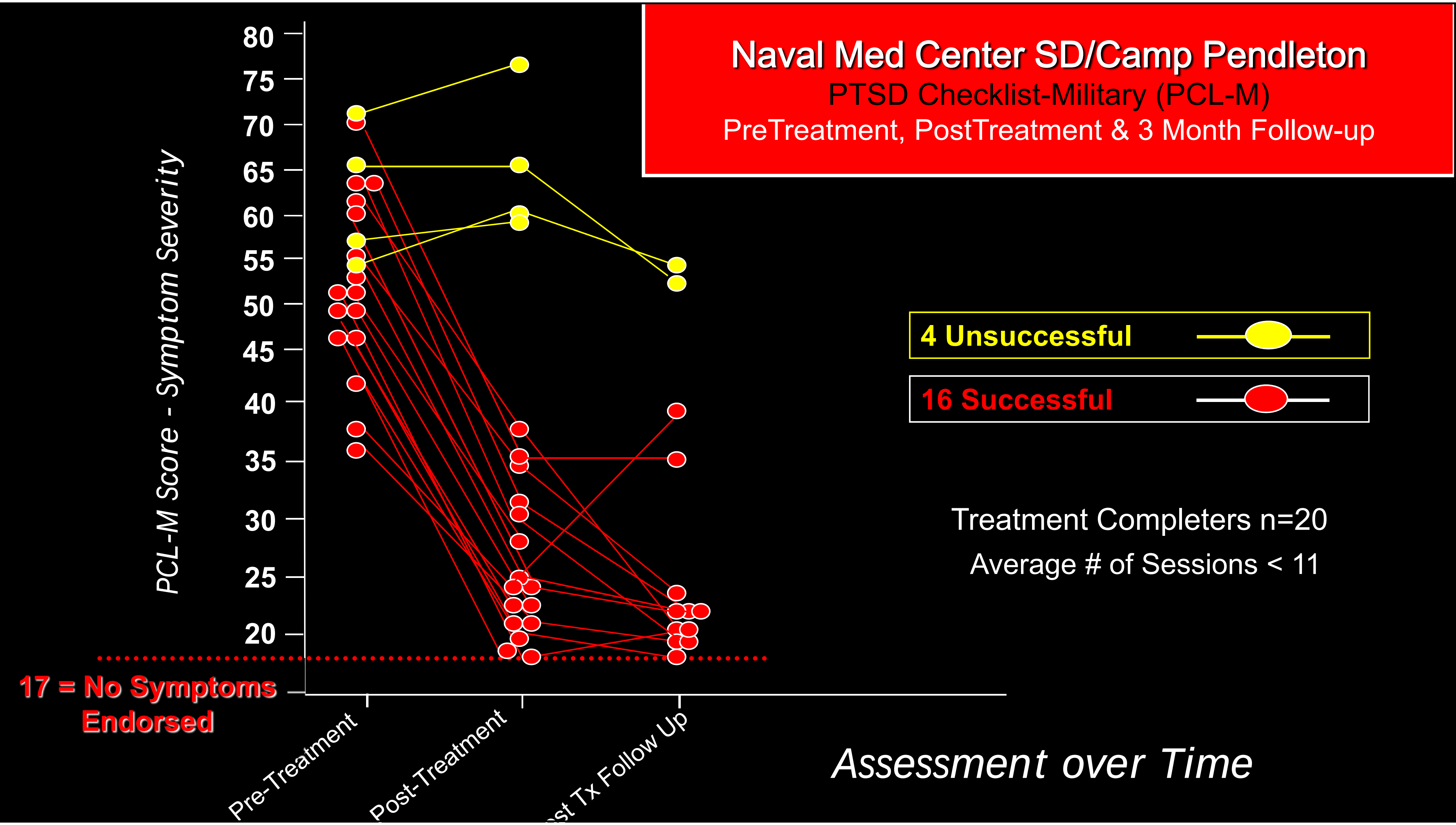
16 of 20 No Longer meet DSM criteria for PTSD at Post-TX



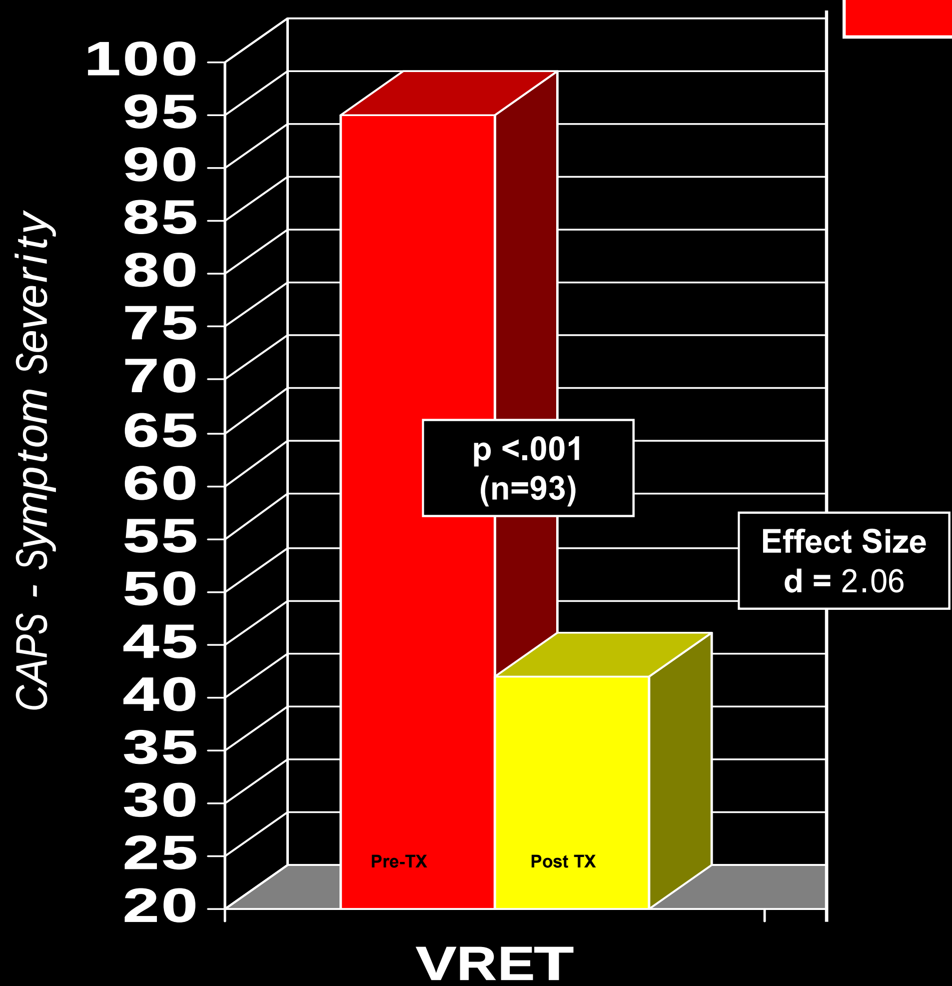
Treatment Completers n=20

Average # of Sessions < 11

In: Rizzo, Difede, Rothbaum & Reger (2010). *Annals of the New York Academy of Sciences*. 1208, 114-125


Naval Med Center SD/Camp Pendleton
PTSD Checklist-Military (PCL-M)
PreTreatment, PostTreatment & 3 Month Follow-up
PCL-M Score - Symptom Severity
80
75
70
65
60
55
50
45
40
35
30
25
20
17 = No Symptoms Endorsed
Pre-Treatment
Post-Treatment
4 Unsuccessful
16 Successful
Treatment Completers n=20
Average # of Sessions < 11
Assessment over Time

Three Week Intensive Treatment combined with Trauma Management Therapy



2017 UNIVERSITY OF CENTRAL FLORIDA

(Beidel et al., 2017, 2019)

Clinician Administered PTSD Scale (CAPS)

PreTreatment & PostTreatment

Treatment Completers n=93

Pre-Treatment

Post-Treatment

Long term Follow-up (3/6months showed that gains were maintained)

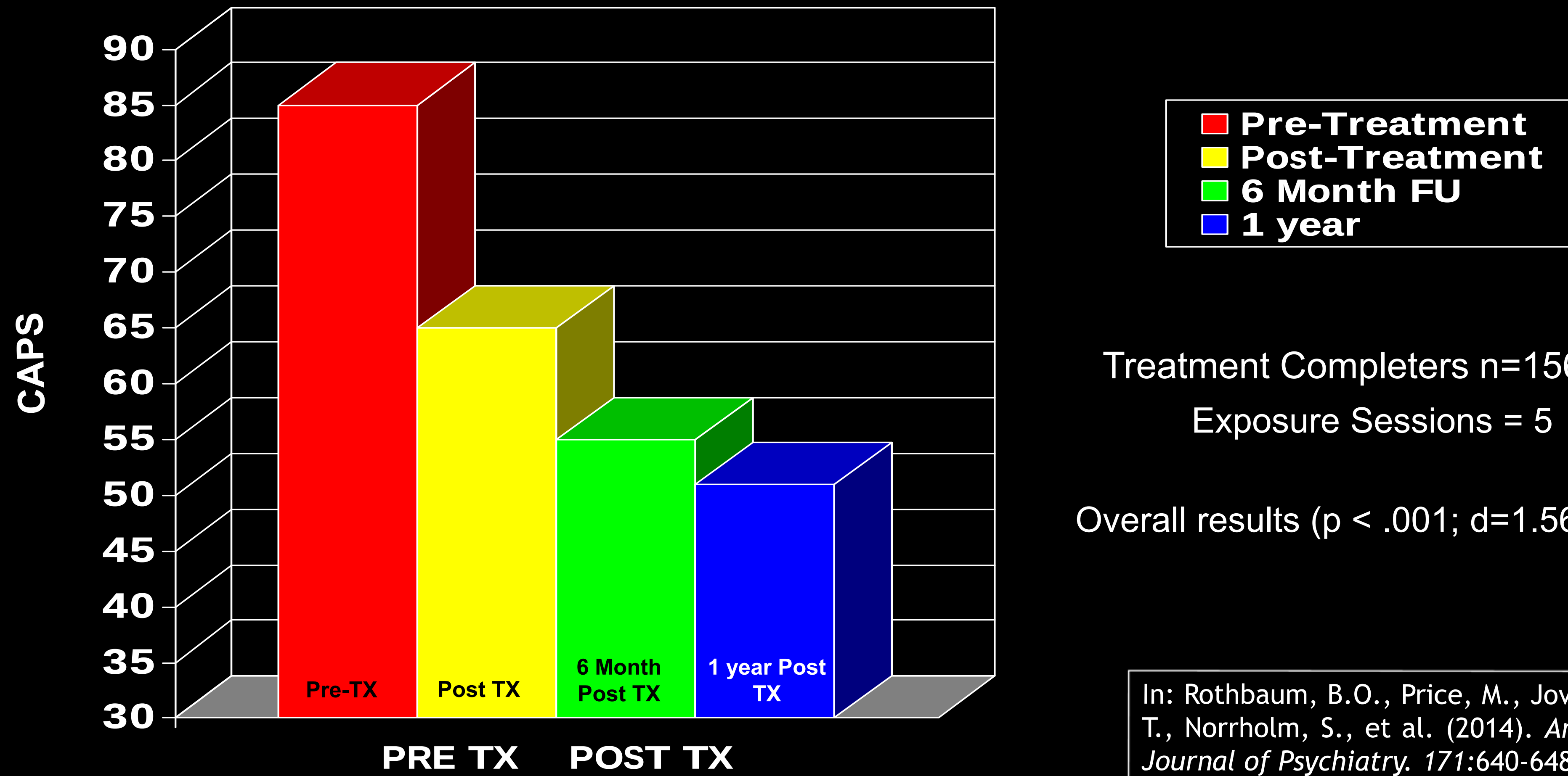
In: Beidel, Frueh, Neer, & Lejuez. (2017). *Journal of Anxiety Disorders*.

Post-Treatment Follow-up to 1 Year

Emory University (Rothbaum et al)

Clinician Administered PTSD Scale (CAPS)

PreTreatment, PostTreatment, 6 Month, & 1 Year Follow-up

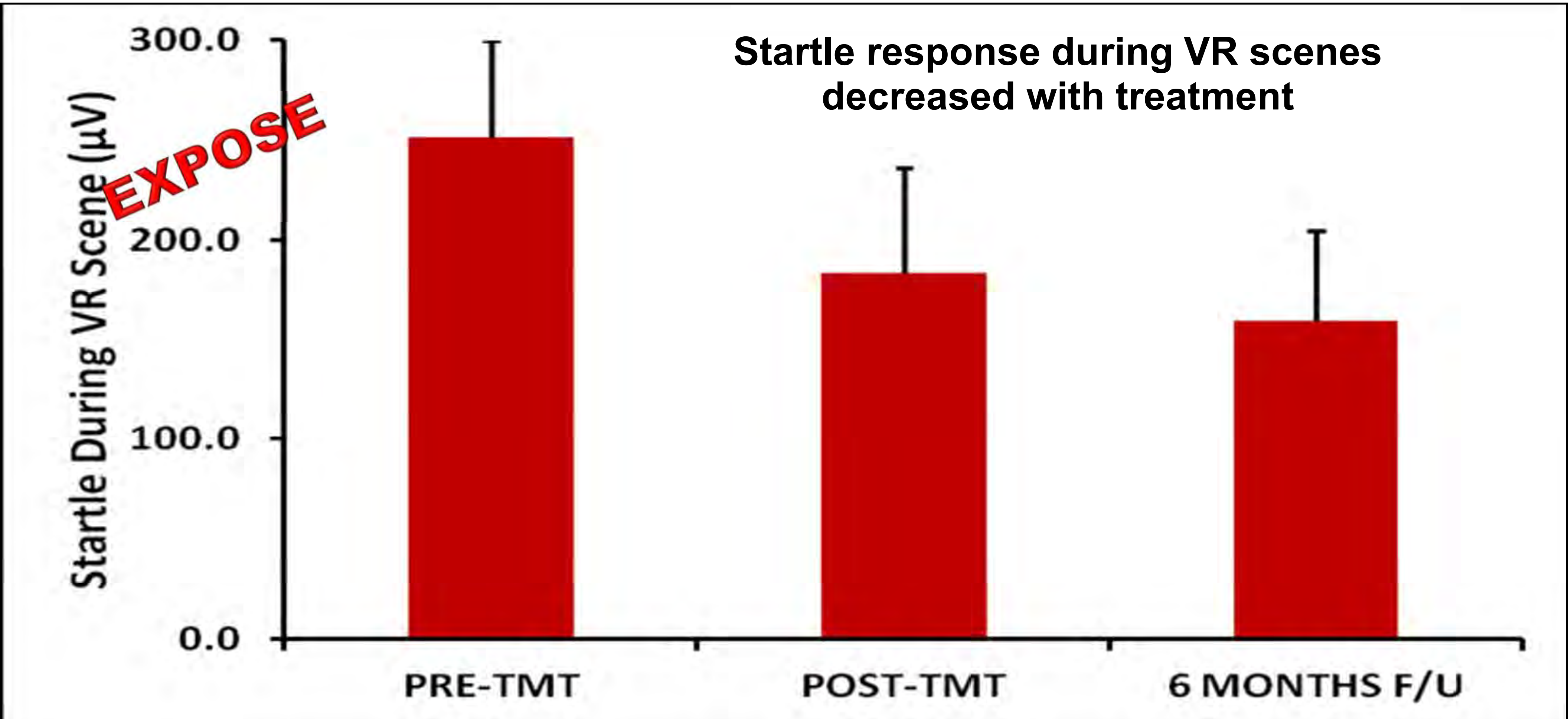


Treatment Completers n=156

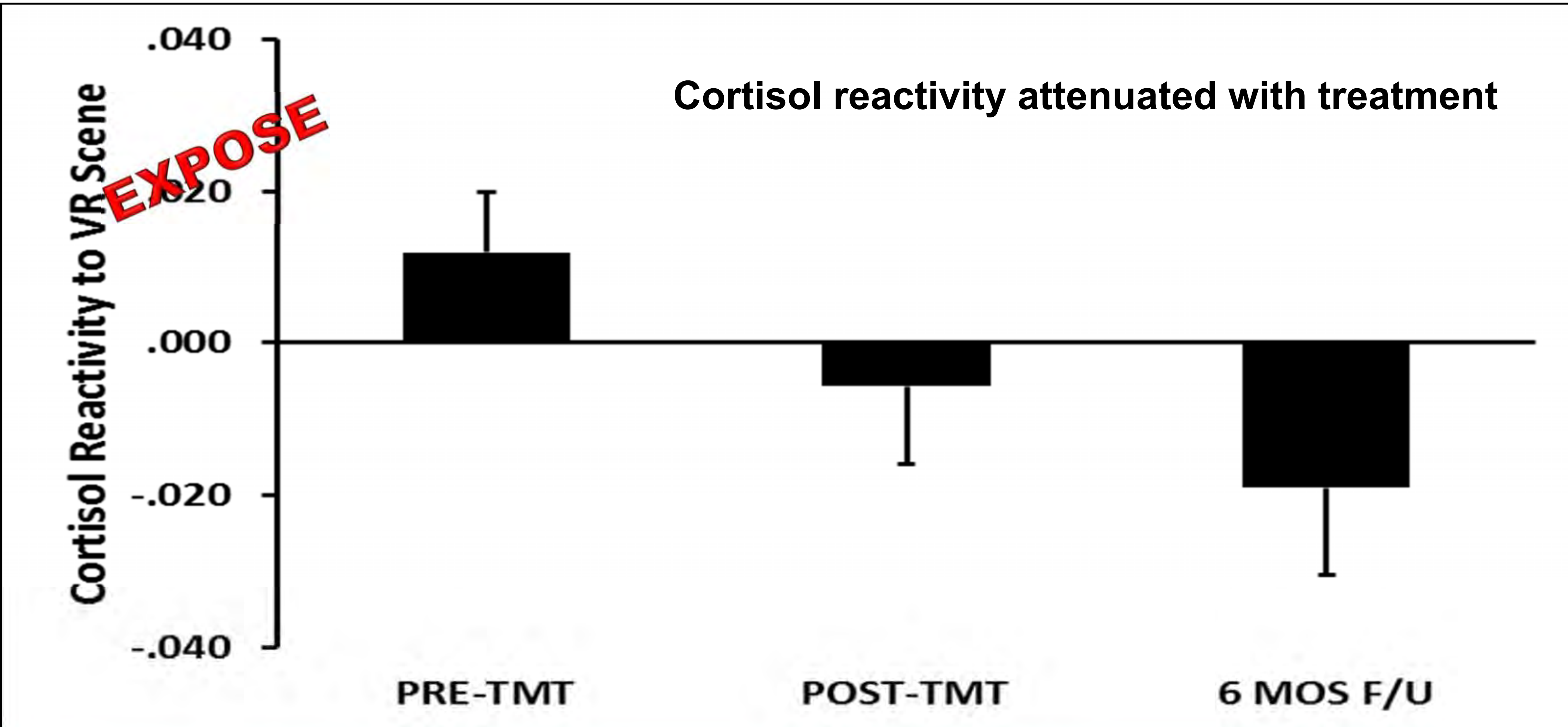
Exposure Sessions = 5

Overall results ($p < .001$; d=1.56)

In: Rothbaum, B.O., Price, M., Jovanovic, T., Norrholm, S., et al. (2014). *American Journal of Psychiatry. 171*:640-648.



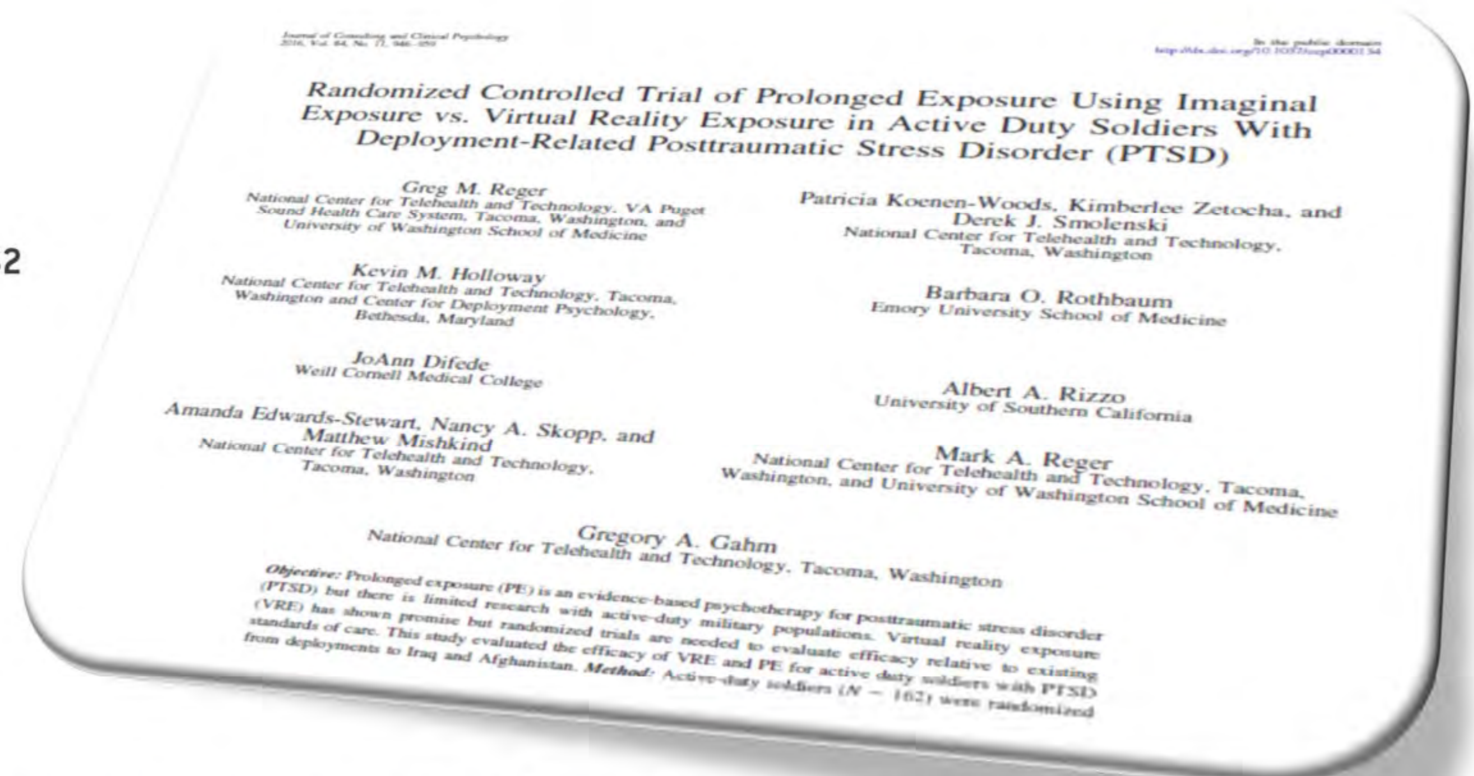
Norrholm, S.D., Jovanovic, T., Gerardi, M., Breazeale, K.G., Davis, M., Duncan, E.J., Ressler, K.J.,Bradley, B., Rizzo, A.A., & Rothbaum, B.O. (2016). Psychophysiological and Cortisol Reactivity as a Predictor of PTSD Treatment Outcome in Virtual Reality Exposure Therapy. *Behaviour Research and Therapy*, 82: 28-37



Norrholm, S.D., Jovanovic, T., Gerardi, M., Breazeale, K.G., Davis, M., Duncan, E.J., Ressler, K.J.,Bradley, B., Rizzo, A.A., & Rothbaum, B.O. (2016). Psychophysiological and Cortisol Reactivity as a Predictor of PTSD Treatment Outcome in Virtual Reality Exposure Therapy. *Behaviour Research and Therapy*, 82: 28-37

In: *Journal of Consulting and Clinical Psychology*

N=162



Journal of Consulting and Clinical Psychology

In the public domain

Randomized Controlled Trial of Prolonged Exposure Using Imaginal Exposure vs. Virtual Reality Exposure in Active Duty Soldiers With Deployment-Related Posttraumatic Stress Disorder (PTSD)

Greg M. Reger
National Center for Telehealth and Technology, VA Puget Sound Health Care System, Tacoma, Washington, and University of Washington School of Medicine

Kevin M. Holloway
National Center for Telehealth and Technology, Tacoma, Washington and Center for Deployment Psychology, Bethesda, Maryland

JoAnn Difede
Weill Cornell Medical College

Amanda Edwards-Stewart, Nancy A. Skopp, and Matthew Mishkind
National Center for Telehealth and Technology, Tacoma, Washington

Patricia Koenen-Woods, Kimberlee Zetocha, and Derek J. Smolenski
National Center for Telehealth and Technology, Tacoma, Washington

Barbara O. Rothbaum
Emory University School of Medicine

Albert A. Rizzo
University of Southern California

Mark A. Reger
National Center for Telehealth and Technology, Tacoma, Washington, and University of Washington School of Medicine

Gregory A. Gahm
National Center for Telehealth and Technology, Tacoma, Washington

Objective: Prolonged exposure (PE) is an evidence-based psychotherapy for posttraumatic stress disorder (PTSD) but there is limited research with active-duty military populations. Virtual reality exposure (VRE) has shown promise but randomized trials are needed to evaluate efficacy relative to existing standards of care. This study evaluated the efficacy of VRE and PE for active duty soldiers with PTSD from deployments to Iraq and Afghanistan. ***Method:*** Active-duty soldiers ($N = 162$) were randomized

Intent-to-treat analyses found that both PE and VRE resulted in significant reductions in PTSD symptoms relative to those in the WL. The majority of patients demonstrated reliable change in PTSD symptoms. PE outperformed VR at 3/6 month FU.

Translational Psychiatry www.nature.com/tp

ARTICLE OPEN

Enhancing exposure therapy for posttraumatic stress disorder (PTSD): a randomized clinical trial of virtual reality and imaginal exposure with a cognitive enhancer

JoAnn Difede[1✉], Barbara O. Rothbaum[2], Albert A. Rizzo[3], Katarzyna Wyka[1], Lisa Spielman[4], Christopher Reist[5,6,7], Michael J. Roy[8], Tanja Jovanovic[9], Seth D. Norrholm[9], Judith Cukor[1], Megan Olden[1], Charles E. Glatt[1] and Francis S. Lee[1]

- **VRET Equivalent to Prolonged Exposure with all Participants**
- **VRET Produced Better Outcomes in PTSD Patients w/Co-morbid Depression**
- **VRET Preferred Prior to Treatment Assignment**

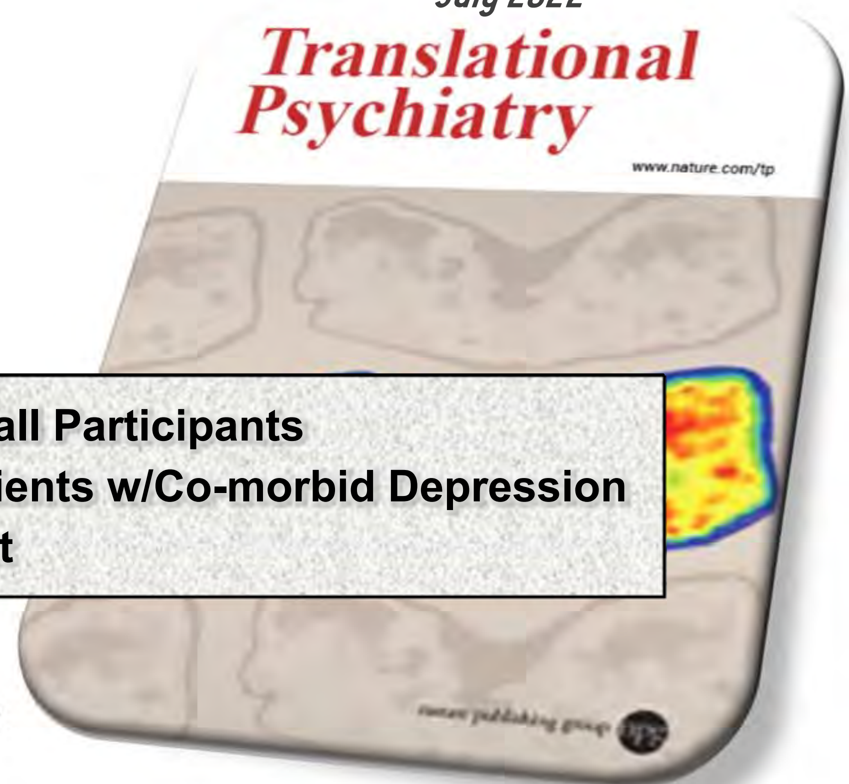
polymorphism on DCS augmentation (ES = 0.67). Met66 allele carriers improved more on DCS (ES = −0.25). FAAH 385 A carriers improved more than non-carriers (ES = 0.33), particularly those with MDD (ES = 0.62). This study provides a step toward precision therapeutics for PTSD by demonstrating that comorbid MDD and genetic markers may help guide treatment selection.

ClinicalTrials.gov Identifier: NCT01352637.

Translational Psychiatry (2022)12:299 ; https://doi.org/10.1038/s41398-022-02066-x

N=192

July 2022



Difede, Rothbaum, Rizzo, Wyka, Spielman, Reist, Roy, Jovanovic, Norrholm, Cukor, Olden, Glatt & Lee (2022)

R&D Spawned from BRAVEMIND

Military Sexual Trauma project

MORE HITCHCOCK THAN HURT LOCKER!

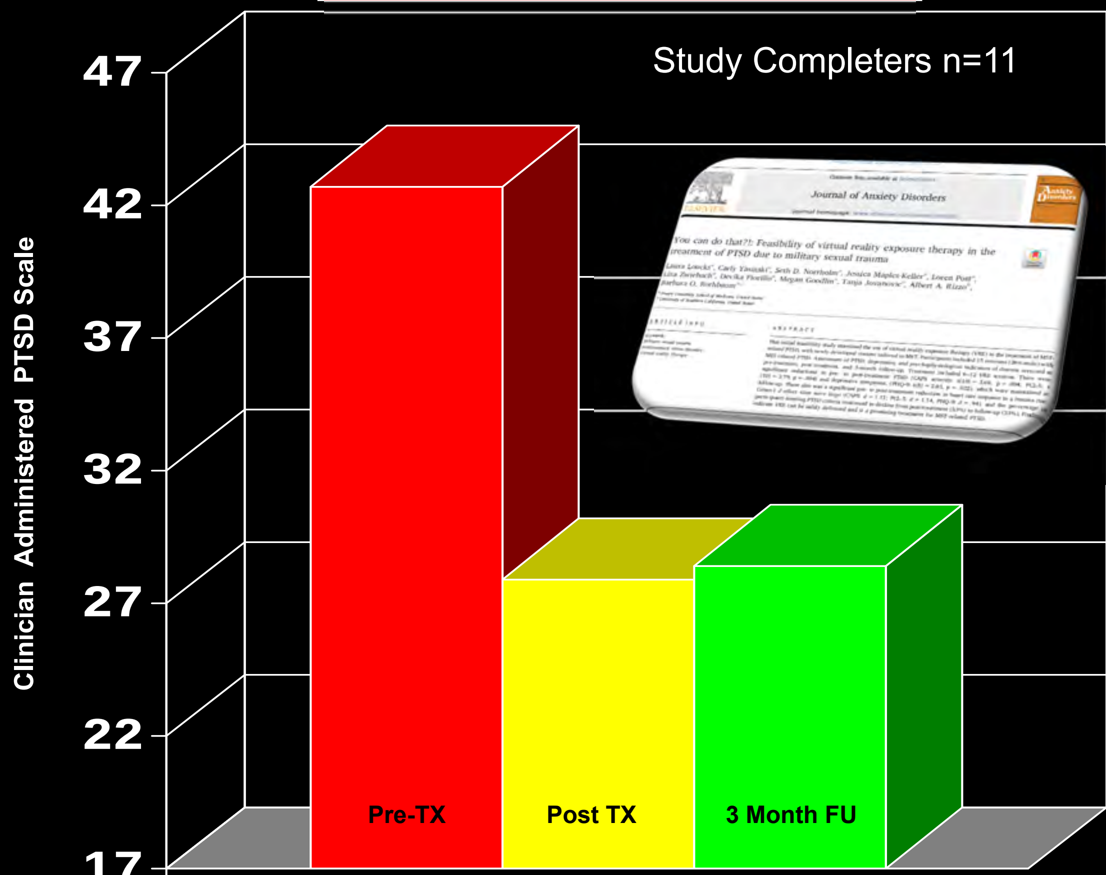
Sexual Trauma content required more advanced "Cinematic" & Civilian Context design effort.

Collaboration with B.O. Rothbaum

PTSD DUE TO MILITARY SEXUAL TRAUMA

Emory Healthcare Veterans Program
Clinician Administered PTSD Scale (CAPS)
PreTreatment, PostTreatment & 3 Month Follow-up

Results from pilot safety/feasibility trial



Paired T-Tests

- CAPS
  - $t(10) = 3.69$, $p = .004$
  - $M_{diff} = 13.64$, $SD_{diff} = 12.27$
- PCL-5
  - $t(10) = 3.79$, $p = .004$
  - $M_{diff} = 20.27$, $SD_{diff} = 17.75$

Effect Size:

- CAPS: Cohens $d = 1.11$
- PCL-5: Cohens $d = 1.14$
- PHQ-9 (Depression) Cohens $d = 0.94$

* Significant pre-post difference on CAPS: $t(9) = 3.81$, $p = .004$; Maintained at 3 month follow-up

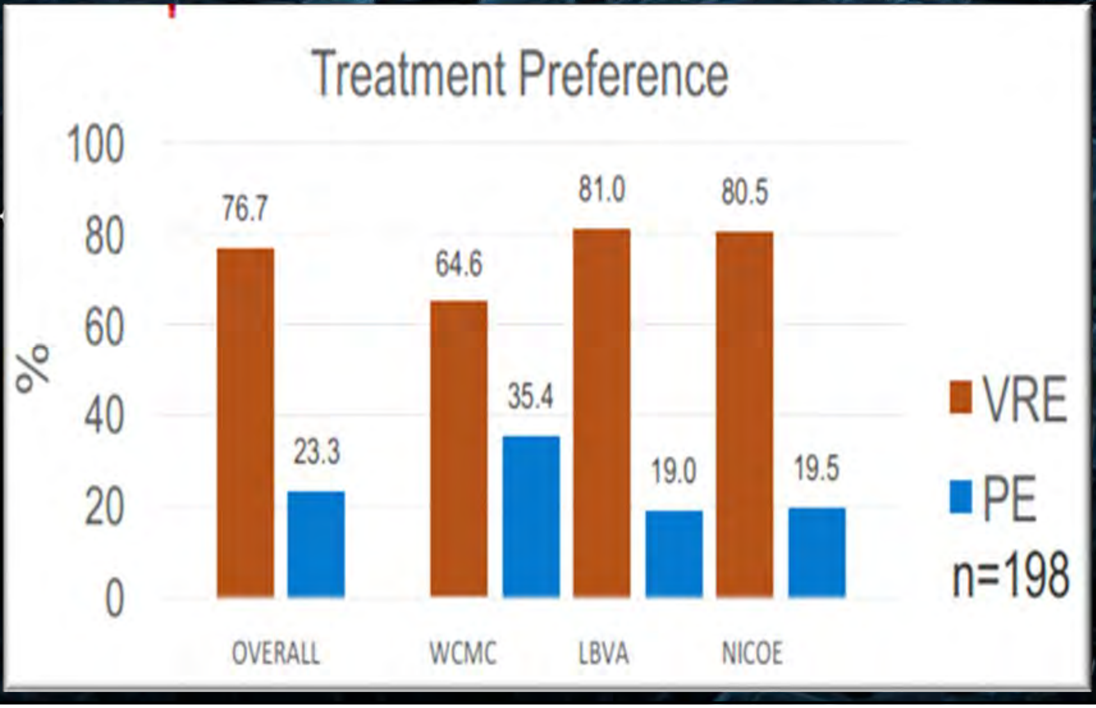
2019

Challenge for Military Healthcare

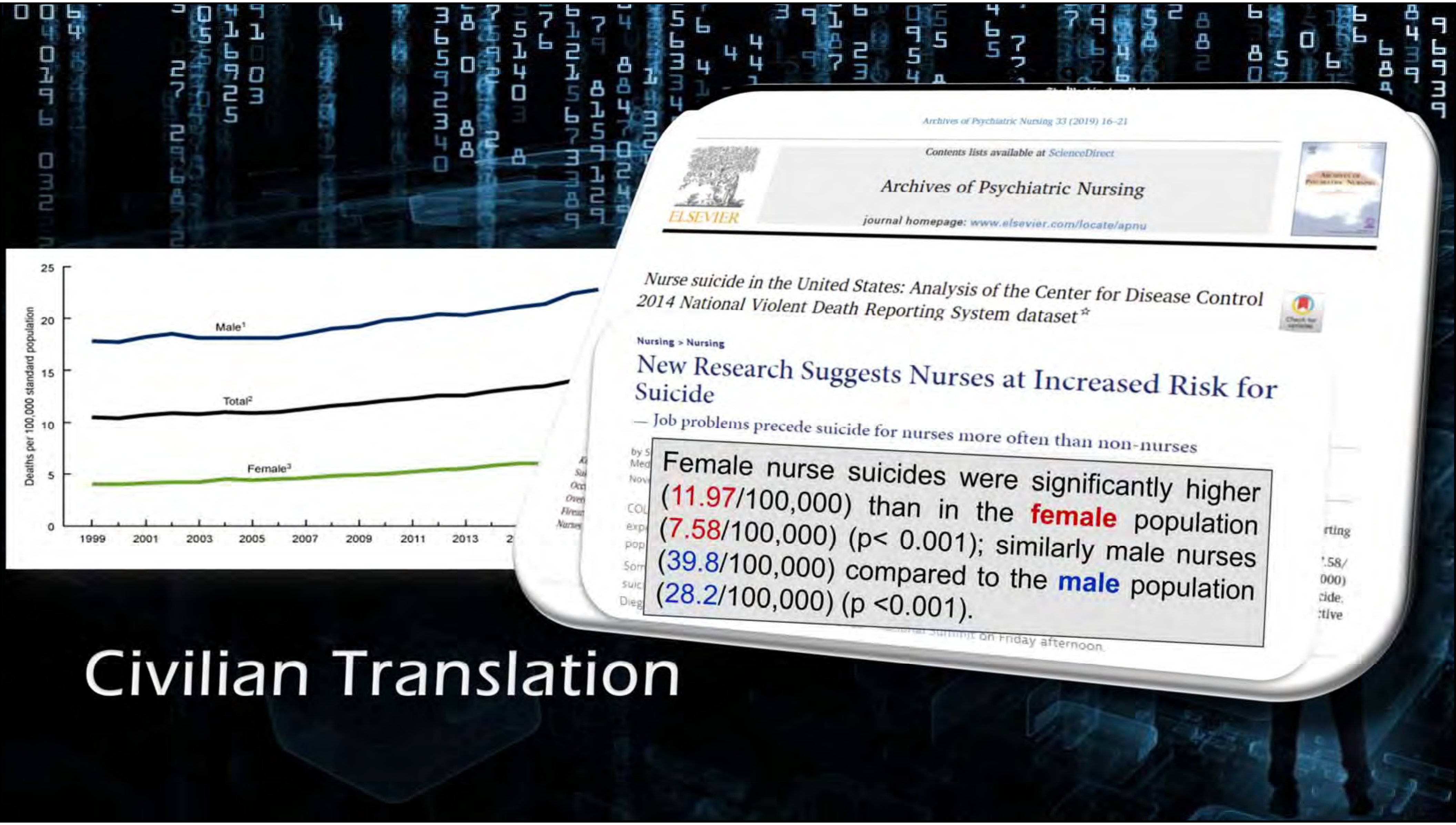
Option: Reconceptualize Therapy → VR Post Deployment Reset Training

Soon to be published: 76.7% of service members in a large RCT (n=198) if given a choice, would pick Virtual Reality over traditional Prolonged Exposure!

MAY APPEAL TO A GENERATION OF SOLDIERS WHO HAVE GROWN UP DIGITAL!

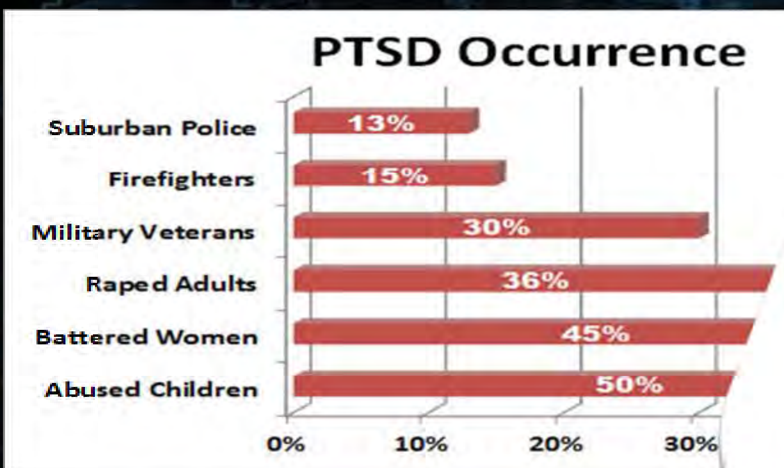


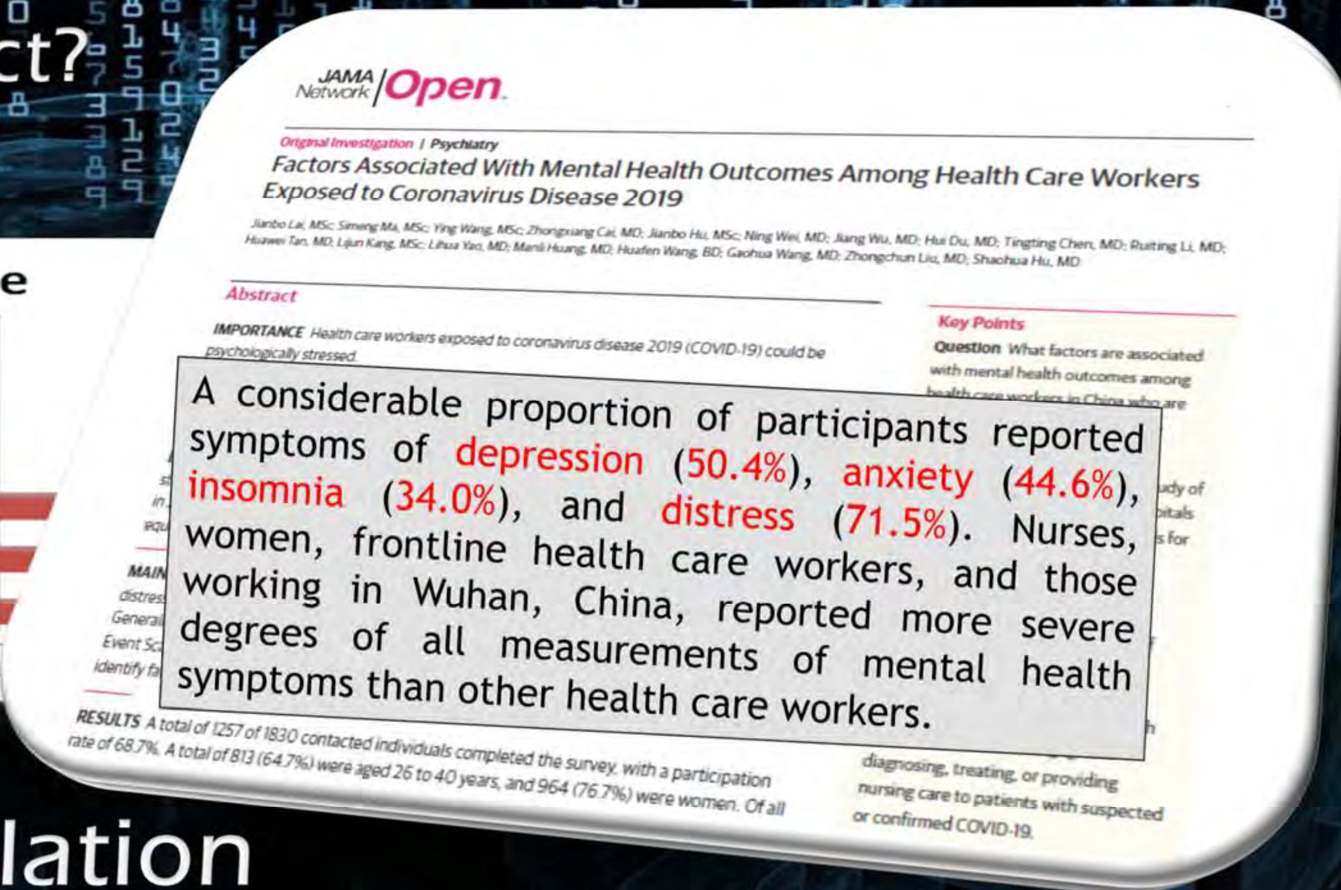

NYC/LAPD Police De-Escalation Project
Suburban P
Firefig
Military Vete
Raped A
Battered Wo
Abused Chil
Correct!
8
7



Archives of Psychiatric Nursing 33 (2019) 16–21
Contents lists available at ScienceDirect
Archives of Psychiatric Nursing
journal homepage: www.elsevier.com/locate/apnu
ELSEVIER
Nurse suicide in the United States: Analysis of the Center for Disease Control 2014 National Violent Death Reporting System dataset☆
Nursing > Nursing
New Research Suggests Nurses at Increased Risk for Suicide
— Job problems precede suicide for nurses more often than non-nurses
Female nurse suicides were significantly higher (11.97/100,000) than in the female population (7.58/100,000) (p< 0.001); similarly male nurses (39.8/100,000) compared to the male population (28.2/100,000) (p <0.001).
Deaths per 100,000 standard population
Male[1]
Total[2]
Female[3]
25
20
15
10
5
0
1999
2001
2003
2005
2007
2009
2011
2013
Civilian Translation

COVID-19 Impact?





JAMA Network | Open.

Original Investigation | Psychiatry

Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019

Jianbo Lai, MSc; Simeng Ma, MSc; Ying Wang, MSc; Zhongxiang Cai, MD; Jianbo Hu, MSc; Ning Wei, MD; Jiang Wu, MD; Hui Du, MD; Tingting Chen, MD; Ruiting Li, MD; Huawei Tan, MD; Lijun Kang, MSc; Lihua Yao, MD; Manli Huang, MD; Huafen Wang, BD; Gaohua Wang, MD; Zhongchun Liu, MD; Shaohua Hu, MD

Abstract

IMPORTANCE Health care workers exposed to coronavirus disease 2019 (COVID-19) could be psychologically stressed.

A considerable proportion of participants reported symptoms of depression (50.4%), anxiety (44.6%), insomnia (34.0%), and distress (71.5%). Nurses, women, frontline health care workers, and those working in Wuhan, China, reported more severe degrees of all measurements of mental health symptoms than other health care workers.

RESULTS A total of 1257 of 1830 contacted individuals completed the survey, with a participation rate of 68.7%. A total of 813 (64.7%) were aged 26 to 40 years, and 964 (76.7%) were women. Of all

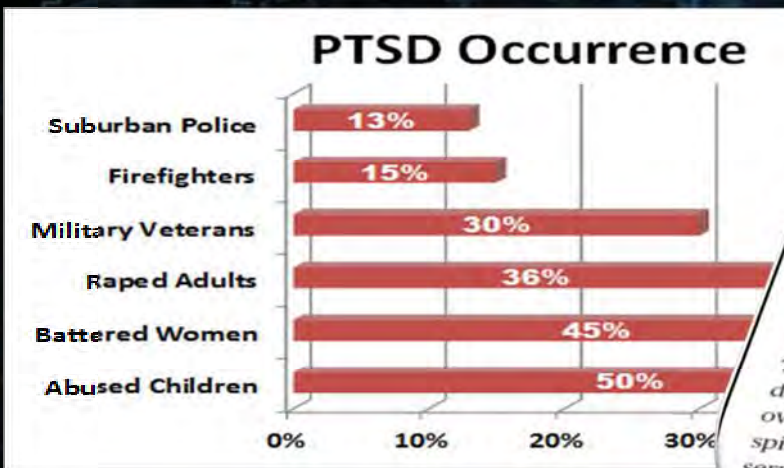
Key Points

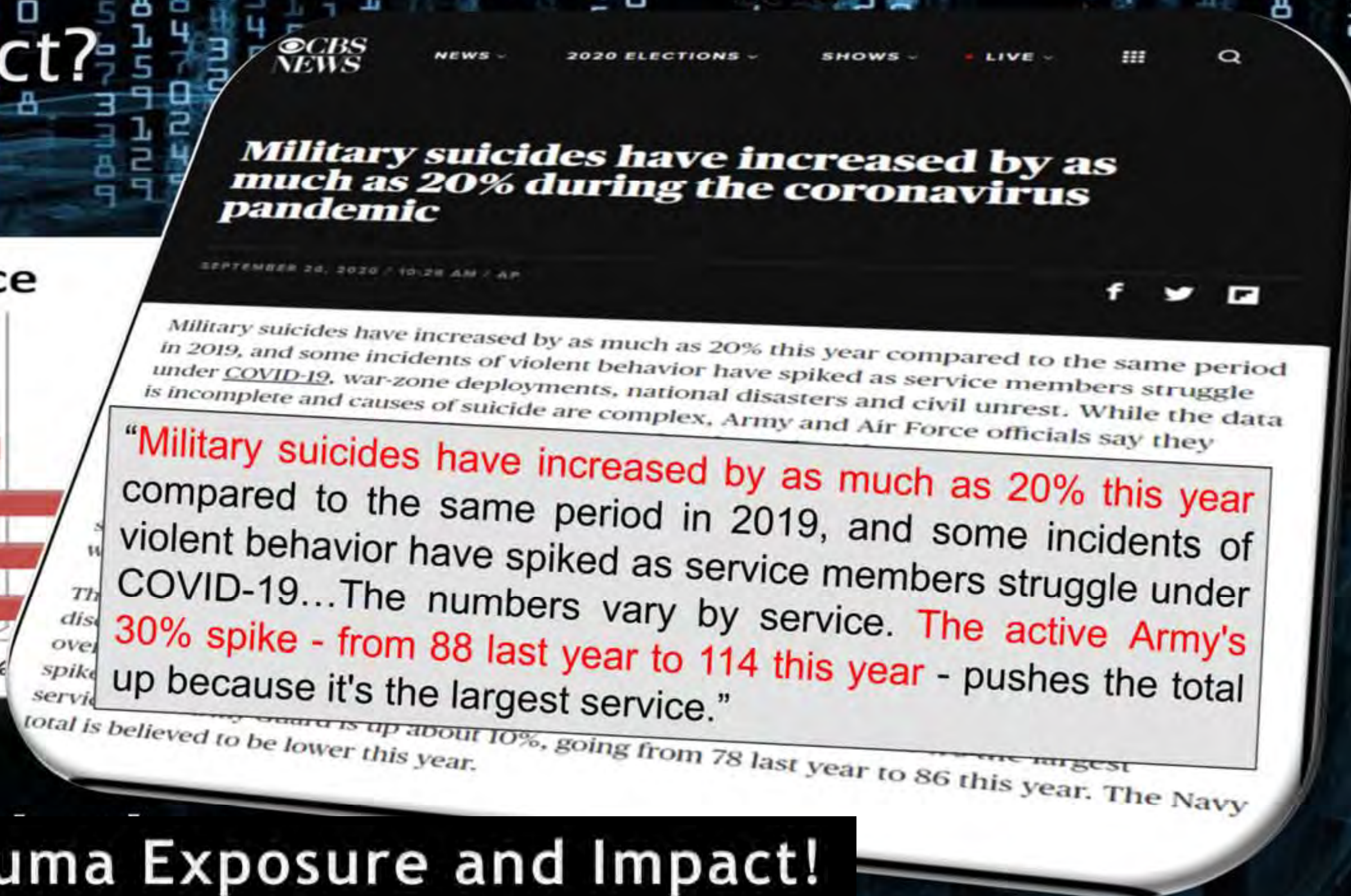
Question What factors are associated with mental health outcomes among health care workers in China who are

diagnosing, treating, or providing nursing care to patients with suspected or confirmed COVID-19.

Civilian Translation

COVID-19 Impact?





CBS NEWS
NEWS
2020 ELECTIONS
SHOWS
LIVE

Military suicides have increased by as much as 20% during the coronavirus pandemic

Military suicides have increased by as much as 20% this year compared to the same period in 2019, and some incidents of violent behavior have spiked as service members struggle under COVID-19, war-zone deployments, national disasters and civil unrest. While the data is incomplete and causes of suicide are complex, Army and Air Force officials say they

"Military suicides have increased by as much as 20% this year compared to the same period in 2019, and some incidents of violent behavior have spiked as service members struggle under COVID-19…The numbers vary by service. The active Army's 30% spike - from 88 last year to 114 this year - pushes the total up because it's the largest service."

… going from 78 last year to 86 this year. The Navy total is believed to be lower this year.

No Shortage of Trauma Exposure and Impact!

The Global Post-

JAMA Network

JAMA Psychiatry

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Research Letter

ONLINE FIRST FREE

February 18, 2021

Posttraumatic Stress Disorder in Patients After Severe COVID-19 Infection

Delfina Janiri, MD[1]; Angelo Carfì, MD[2]; Georgios D. Kotzalidis, MD, PhD[1]; et al

Author Affiliations | Article Information

JAMA Psychiatry. Published online February 18, 2021. doi:10.1001/jamapsychiatry.2021.0109

Read & annotate PDF + Add to wizdom.ai

Posttraumatic stress disorder (PTSD) may occur in individuals who have experienced a traumatic event. Previous coronavirus epidemics were associated with PTSD diagnoses in postillness stages, with meta-analytic findings indicating a prevalence of 32.2% (95% CI, 23.7-42.0).[1] However, information after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is piecemeal. We aimed at filling this gap by studying a group of patients with coronavirus disease 2019 (COVID-19) who sought treatment at the emergency department, most of whom required hospitalization, eventually recovered, and were subsequently referred to a postacute care service for multidisciplinary assessment.

GlobeNewswire January 28, 2020

Global Post-Traumatic Stress Disorder (PSTD) Therapeutics Market 2020-2024

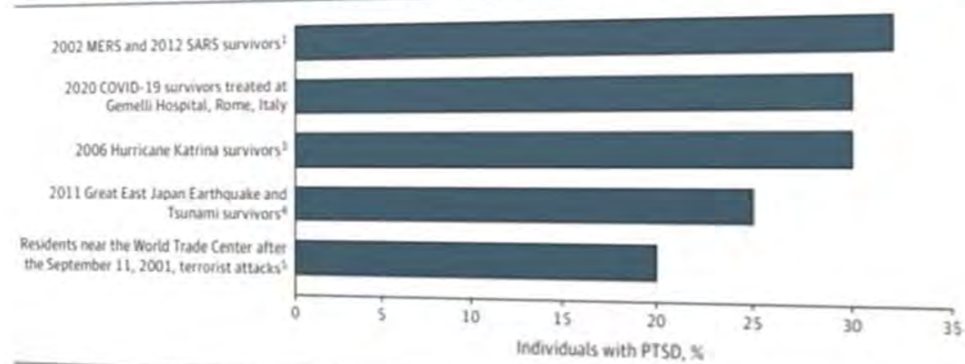
analyst has been monitoring the global post-tra...

Treatment

Dovepress

ASE SERIES

Figure. Posttraumatic Stress Disorder (PTSD) After COVID-19 Infection and Other Collective Traumatic Events



) therapeutics market as well.

Segmentation

The global post-traumatic stress disorder (PSTD) therapeutics market is segmented as below:

Product

• Other PSTD therapeutics

of

de

he

ds.

No Shortage of Trauma Exposure and Impact!

CROSS-PLATFORM WELLNESS SUPPORT SYSTEM

Integrated Virtual Reality and Virtual Human Interactive Systems to Maintain Mental Health and Wellness

Albert "Skip" Rizzo, Sharon Mozgai, David Kwok,
Andrew Leeds, Brett Talbot & Arno Hartholt

Tech translation from Military to Civilian needs!


CROSS-PLATFORM WELLNESS SUPPORT SYSTEM
Integrated Virtual Reality and Virtual Human Interactive Systems to Maintain Mental Health and Wellness
Albert "Skip" Rizzo, Sharon Mozgai, David Kwok, Andrew Leeds, Brett Talbot & Arno Hartholt
VR Exposure Therapy
Mobile Health & Wellness App
Professional Quality of Life Scale (ProQOL)
Technologies
University of Southern California
Online Healthcare Professional Burnout Coach
Analysis of
Video
MASSACHUSETTS GENERAL HOSPITAL
ConverSage
15:02
VR Mindfulness/Meditation
Tech translation from Military to Civilian needs!

Clinical Targets

- PTSD
- Professional Burnout
- Anxiety
- Depression
- Grief & Loss
- Addiction
- Sleep Disturbances
- Anger Management
- Loneliness
- General Wellness

FOR MORE DETAIL

Rizzo, A., Hartholt, A. & Mozgai, S. (in press). Virtual Reality and PTSD: From Combat to COVID-19 to Cops and Beyond. In: Greenleaf, W. & Fine, R. (eds,) Applied Virtual Reality in Healthcare: Case Studies and Perspectives. Cool Blue Media, Washington D.C.


Applied Virtual Realty in Healthcare: Case Studies and Perspectives
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Title: Applied Virtual Reality in Healthcare: Case Studies and Perspectives
Edited By: Dr. Walter Greenleaf and Robert Fine
Foreword: Palmer Luckey
Preorder Launch Date: Dec. 14, 2020
Retail: $40.99 USD
Release: March '21

https://appliedvirtualrealityinhealthcare.com/

USC Institute for Creative Technologies

The Ukraine Project

Metaverse Prototype for VRET application to address longer term PTS needs.

University of Bucharest

FDL

Fountain Digital Labs

agora

USC Institute for Creative Technologies

The Ukraine Project

UNIVERSITY OF BUCHAREST

Metaverse Prototype for Social Support applications to address more immediate refugee community needs using spherical imagery

Avatar Styles

FDL Fountain Digital Labs

A Mental Health Tsunami on the Horizon?

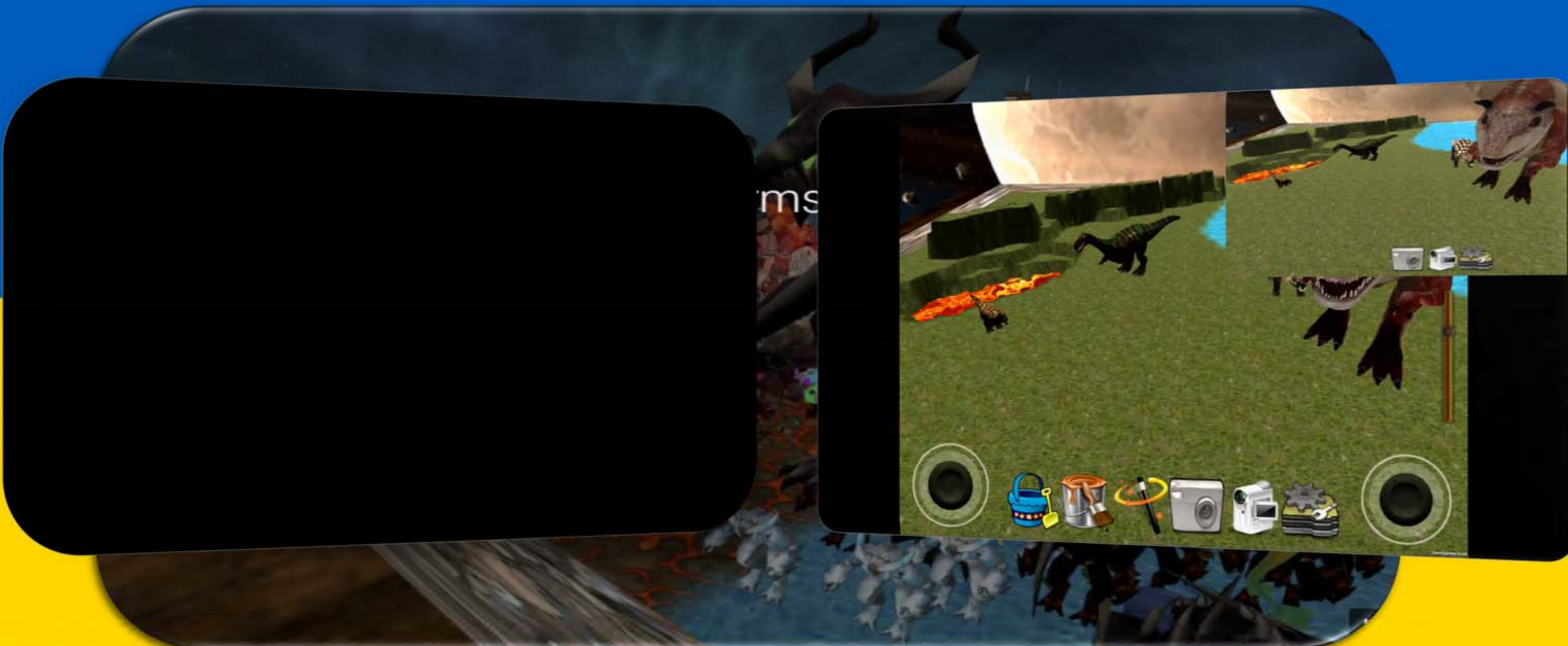
agora

USC Institute for Creative Technologies

UNIVERSITY OF BUCHAREST

Virtual Sandtray

An Immersive Storytelling Tool for Supporting Traumatized Children Construction of Trauma Narratives



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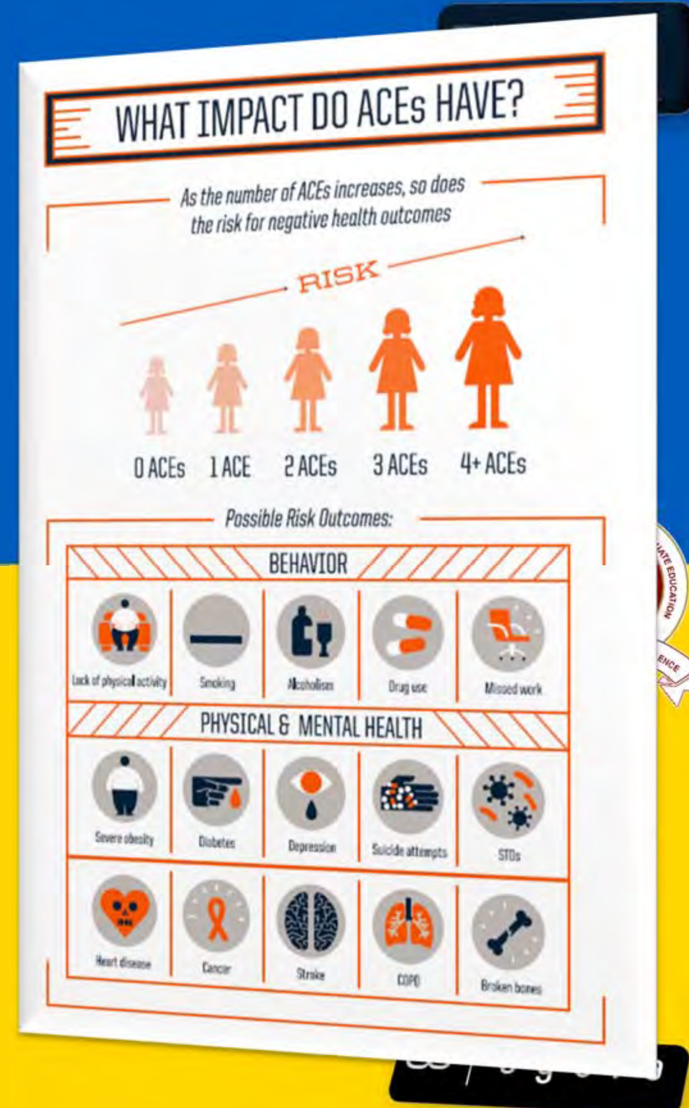
Jessica Stone, Ph.D.

VIRTUAL SANDTRAY

agora

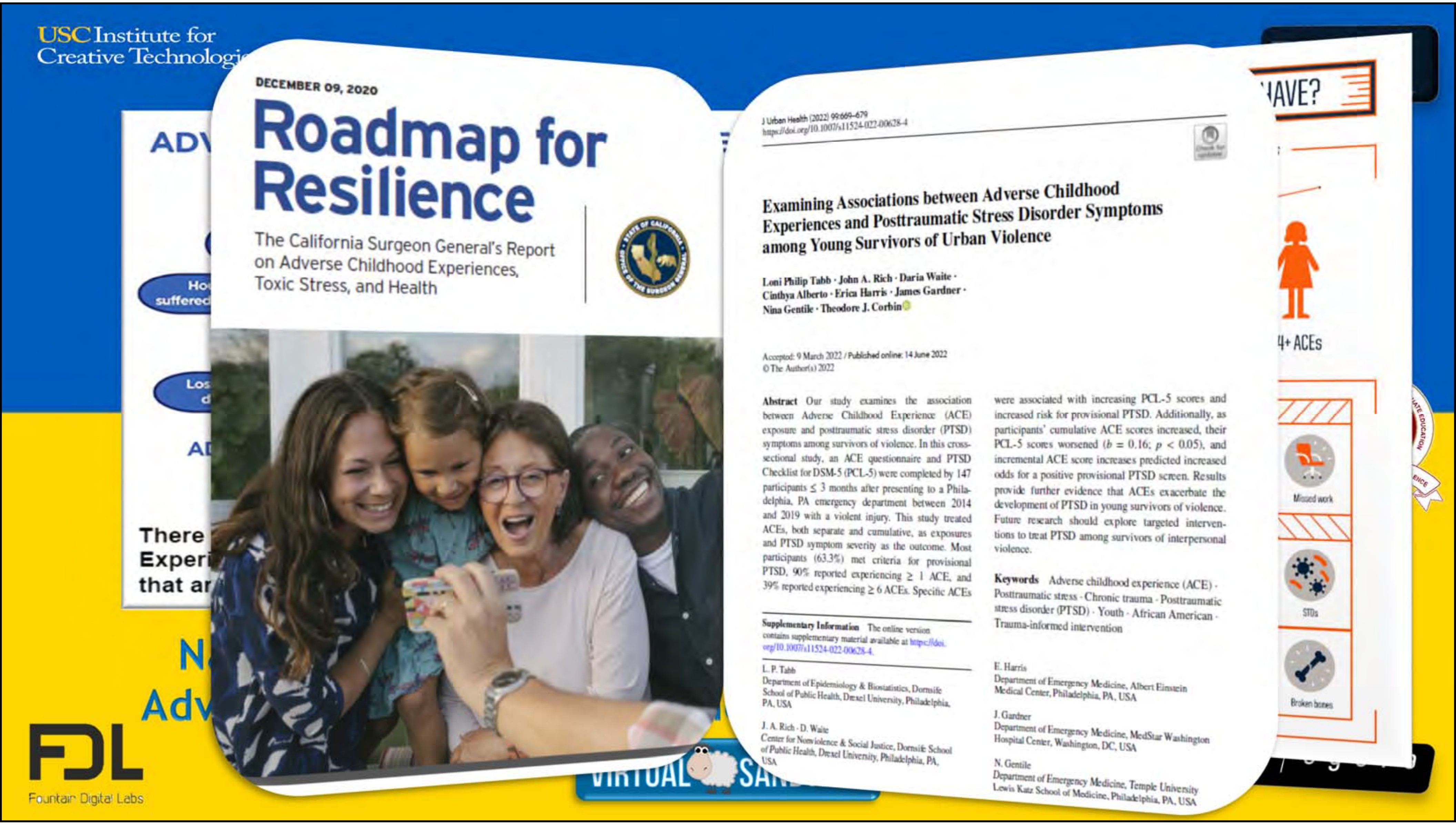
USC Institute for Creative Technologies



Narrative Play Therapy to Address Adverse Childhood Experiences (ACE)

FDL
Fountain Digital Labs

VIRTUAL SANDTRAY


USC Institute for
Creative Technologi
DECEMBER 09, 2020
Roadmap for Resilience
The California Surgeon General's Report on Adverse Childhood Experiences, Toxic Stress, and Health
J Urban Health (2022) 99:669–679
https://doi.org/10.1007/s11524-022-00628-4
Examining Associations between Adverse Childhood Experiences and Posttraumatic Stress Disorder Symptoms among Young Survivors of Urban Violence
Loni Philip Tabb · John A. Rich · Daria Waite · Cinthya Alberto · Erica Harris · James Gardner · Nina Gentile · Theodore J. Corbin
Accepted: 9 March 2022 / Published online: 14 June 2022
© The Author(s) 2022
Abstract Our study examines the association between Adverse Childhood Experience (ACE) exposure and posttraumatic stress disorder (PTSD) symptoms among survivors of violence. In this cross-sectional study, an ACE questionnaire and PTSD Checklist for DSM-5 (PCL-5) were completed by 147 participants ≤ 3 months after presenting to a Philadelphia, PA emergency department between 2014 and 2019 with a violent injury. This study treated ACEs, both separate and cumulative, as exposures and PTSD symptom severity as the outcome. Most participants (63.3%) met criteria for provisional PTSD, 90% reported experiencing ≥ 1 ACE, and 39% reported experiencing ≥ 6 ACEs. Specific ACEs were associated with increasing PCL-5 scores and increased risk for provisional PTSD. Additionally, as participants' cumulative ACE scores increased, their PCL-5 scores worsened ($b = 0.16$; $p < 0.05$), and incremental ACE score increases predicted increased odds for a positive provisional PTSD screen. Results provide further evidence that ACEs exacerbate the development of PTSD in young survivors of violence. Future research should explore targeted interventions to treat PTSD among survivors of interpersonal violence.
Keywords Adverse childhood experience (ACE) · Posttraumatic stress · Chronic trauma · Posttraumatic stress disorder (PTSD) · Youth · African American · Trauma-informed intervention
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11524-022-00628-4.
L. P. Tabb
Department of Epidemiology & Biostatistics, Dornsife School of Public Health, Drexel University, Philadelphia, PA, USA
J. A. Rich · D. Waite
Center for Nonviolence & Social Justice, Dornsife School of Public Health, Drexel University, Philadelphia, PA, USA
E. Harris
Department of Emergency Medicine, Albert Einstein Medical Center, Philadelphia, PA, USA
J. Gardner
Department of Emergency Medicine, MedStar Washington Hospital Center, Washington, DC, USA
N. Gentile
Department of Emergency Medicine, Temple University Lewis Katz School of Medicine, Philadelphia, PA, USA
4+ ACEs
Missed work
STDs
Broken bones
FDL
Fountain Digital Labs


3. Experience Less Pain
VR Pain Management

The New York Times

Virtual Reality as Therapy for Pain

It's more than a distraction, researchers say. It's more like a brain hack that occupies the brain so fully that it has no room to process pain sensations at the same time.

Gracia Lam

Theoretical Basis: *VR/Games Pain Distraction*

Limited-Capacity of Attention

(e.g., Broadbent, 1958; Shiffrin & Schneider, 1977; McCaul & Malott, 1984)

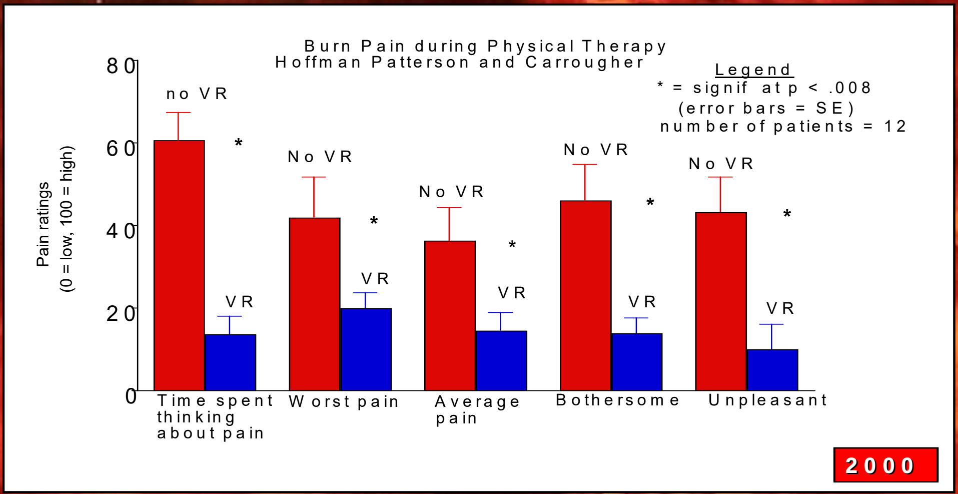
Like a Spotlight

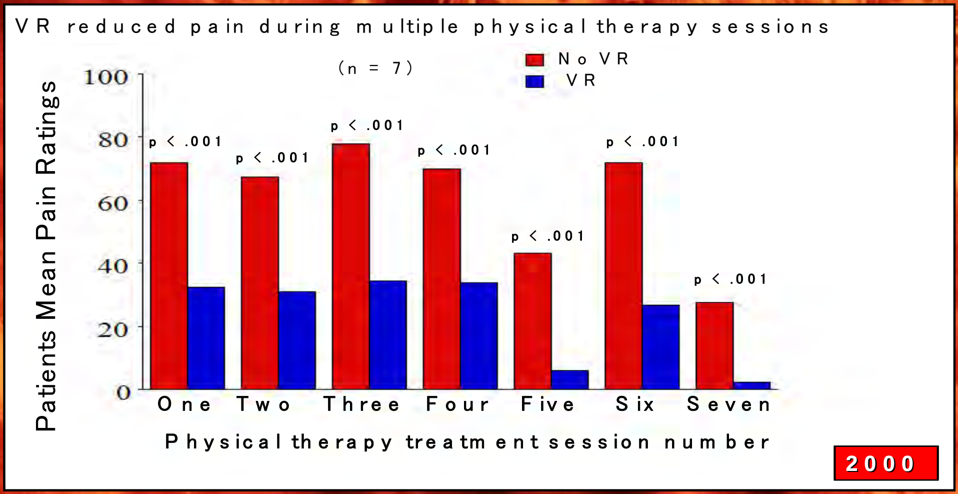
Attention and Pain

- Pain perception requires attending to noxious stimuli
- Pain can be reduced by distributing attention elsewhere
- Effectiveness related to intensity, novelty, & unpredictability of distracting stimuli
- VR/Games draws heavily upon attentional resources
- HMD prevents visual perception of environment

DISTRACT

Nintendo vs. Immersive VR





VR Distraction Reduces Acute Pain Perception

VR Distraction Effect Continues Over Time

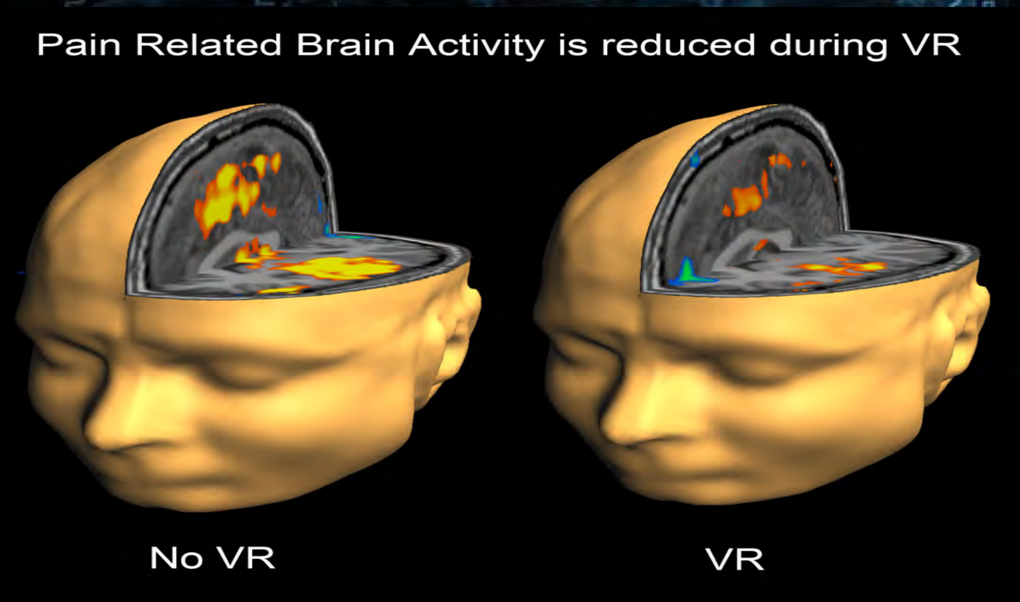
These Findings have been consistently replicated and extended over the last 20 years!

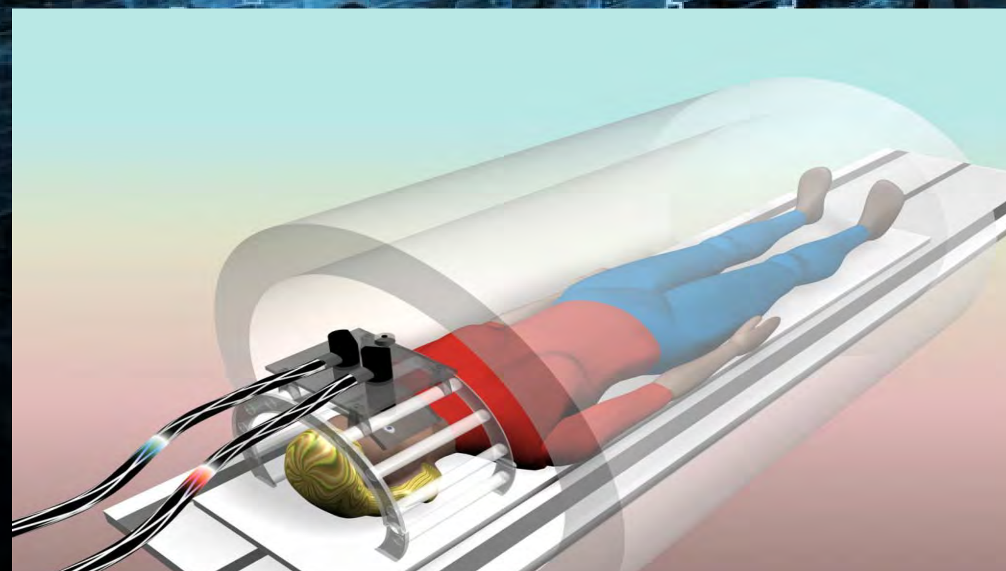
DISTRACT

2000-2018

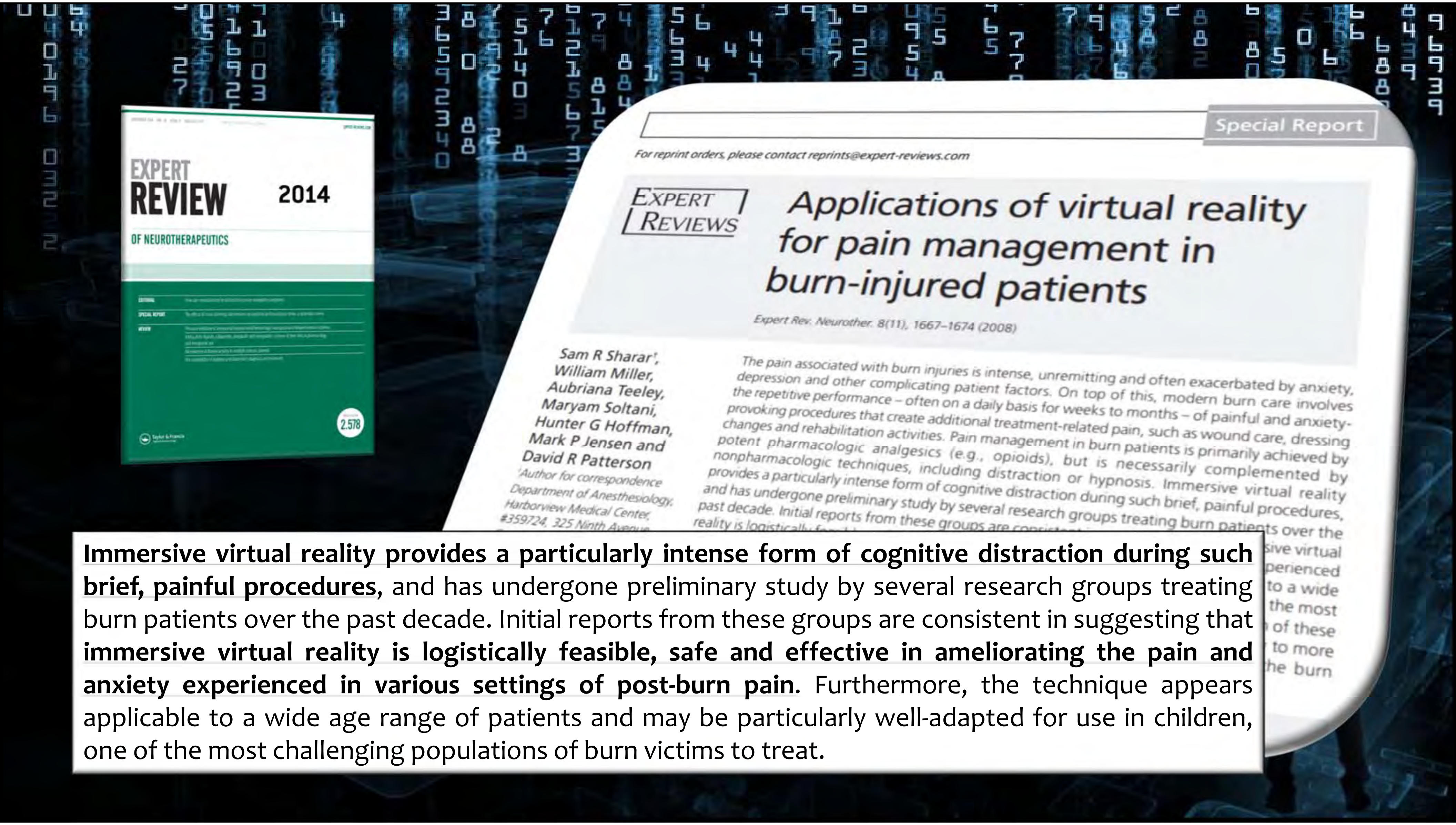
fMRI VR Pain Distraction

(Hoffman et al.)

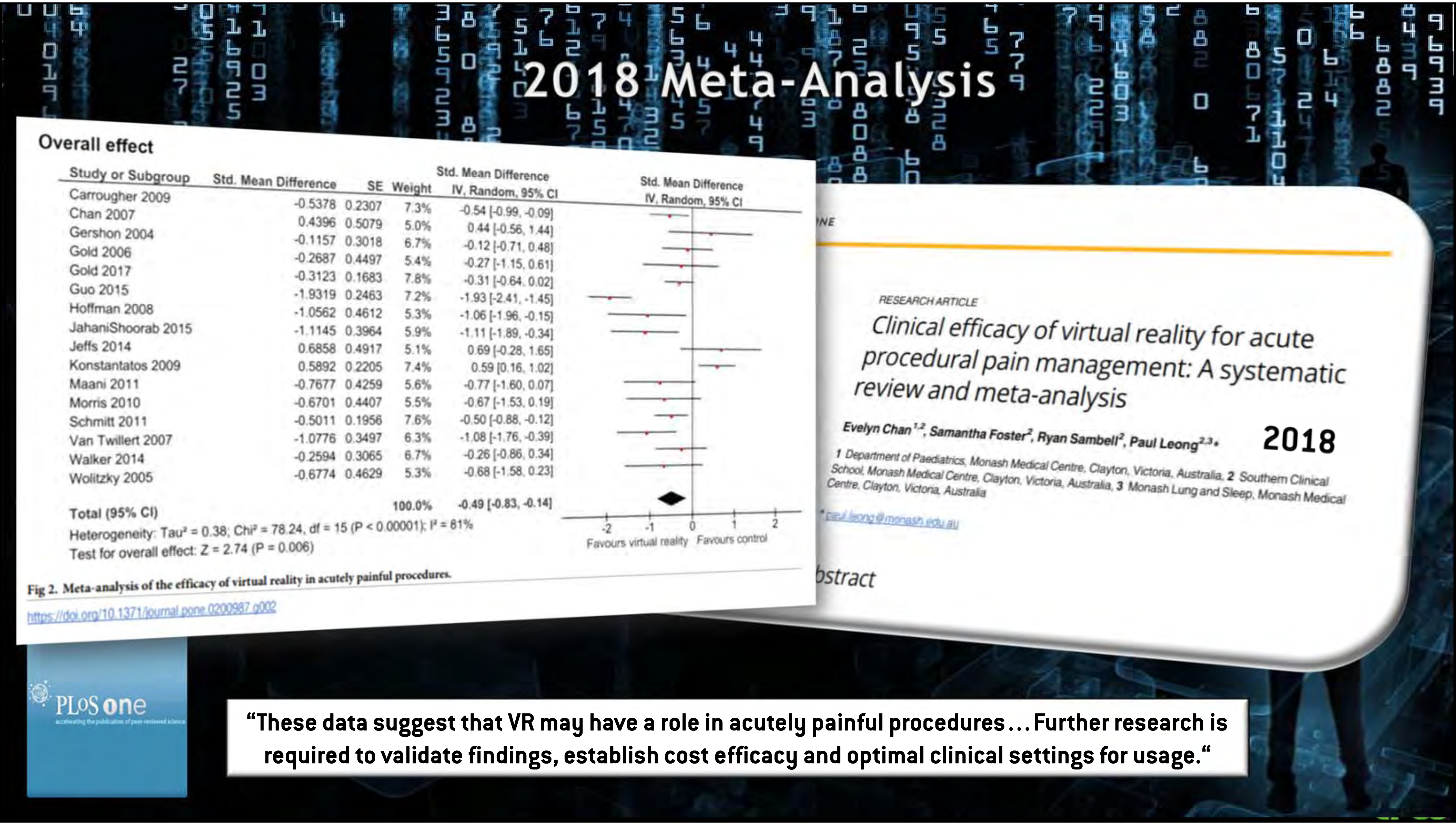




Reduced Activation in: Primary & Secondary Somatosensory Cortex, Anterior Cingulate, Thalamus and Insula



Immersive virtual reality provides a particularly intense form of cognitive distraction during such brief, painful procedures, and has undergone preliminary study by several research groups treating burn patients over the past decade. Initial reports from these groups are consistent in suggesting that **immersive virtual reality is logistically feasible, safe and effective in ameliorating the pain and anxiety experienced in various settings of post-burn pain**. Furthermore, the technique appears applicable to a wide age range of patients and may be particularly well-adapted for use in children, one of the most challenging populations of burn victims to treat.

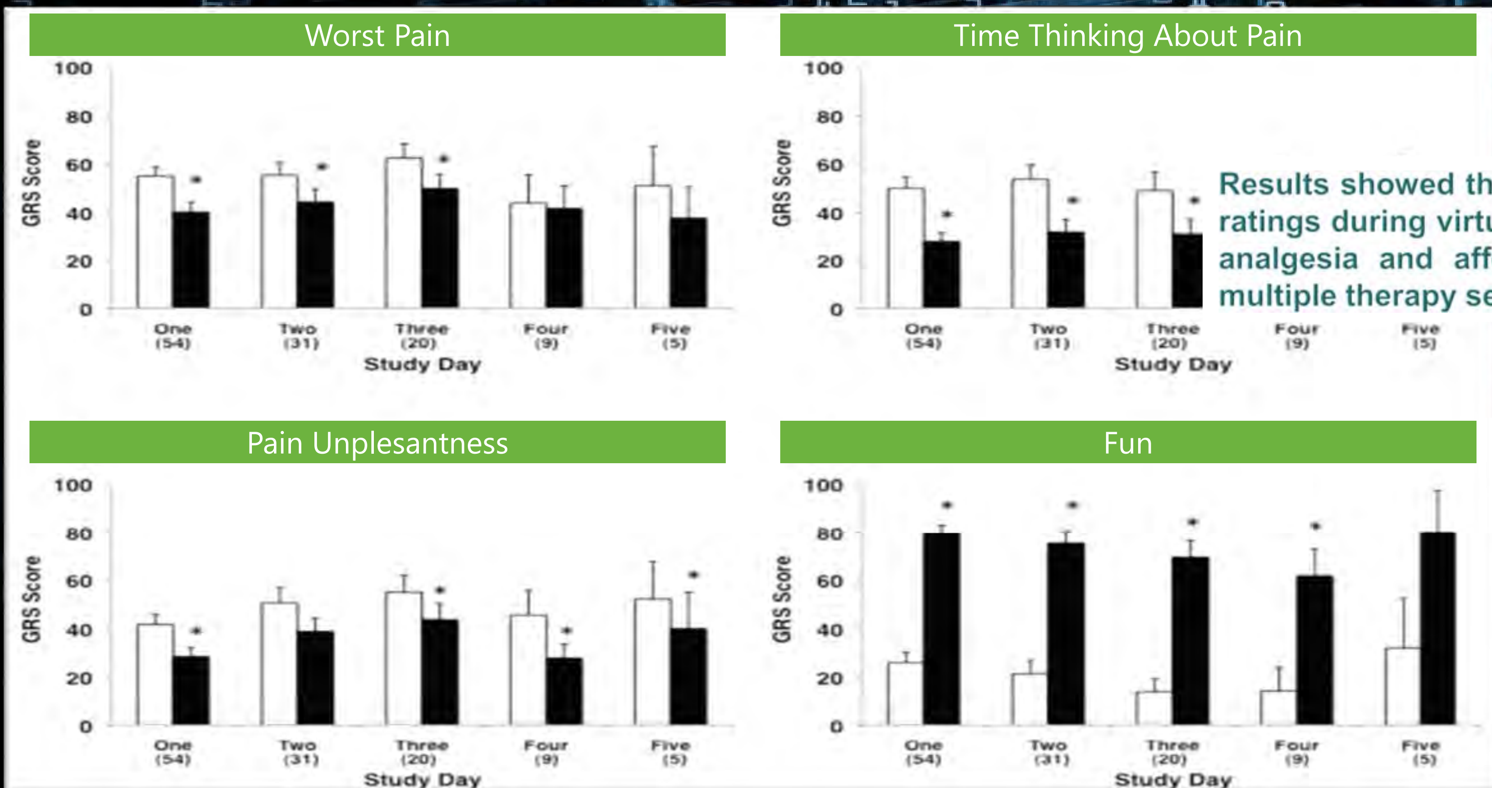


Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI
Carrougher 2009	-0.5378	0.2307	7.3%	-0.54 [-0.99, -0.09]
Chan 2007	0.4396	0.5079	5.0%	0.44 [-0.56, 1.44]
Gershon 2004	-0.1157	0.3018	6.7%	-0.12 [-0.71, 0.48]
Gold 2006	-0.2687	0.4497	5.4%	-0.27 [-1.15, 0.61]
Gold 2017	-0.3123	0.1683	7.8%	-0.31 [-0.64, 0.02]
Guo 2015	-1.9319	0.2463	7.2%	-1.93 [-2.41, -1.45]
Hoffman 2008	-1.0562	0.4612	5.3%	-1.06 [-1.96, -0.15]
JahaniShoorab 2015	-1.1145	0.3964	5.9%	-1.11 [-1.89, -0.34]
Jeffs 2014	0.6858	0.4917	5.1%	0.69 [-0.28, 1.65]
Konstantatos 2009	0.5892	0.2205	7.4%	0.59 [0.16, 1.02]
Maani 2011	-0.7677	0.4259	5.6%	-0.77 [-1.60, 0.07]
Morris 2010	-0.6701	0.4407	5.5%	-0.67 [-1.53, 0.19]
Schmitt 2011	-0.5011	0.1956	7.6%	-0.50 [-0.88, -0.12]
Van Twillert 2007	-1.0776	0.3497	6.3%	-1.08 [-1.76, -0.39]
Walker 2014	-0.2594	0.3065	6.7%	-0.26 [-0.86, 0.34]
Wolitzky 2005	-0.6774	0.4629	5.3%	-0.68 [-1.58, 0.23]
Total (95% CI)			100.0%	-0.49 [-0.83, -0.14]


Pain Distraction Scenarios
appliedVR
Firsthand TECHNOLOGY
SkyRim
GLOW!
Firsthand TECHNOLOGY
Firsthand TECHNOLOGY
VRMC
Tuscany Tour

What About Younger Clients...

A Randomized, Controlled Trial of Immersive Virtual Reality Analgesia during Physical Therapy for Pediatric Burn Injuries



Results showed that on study day one, subjects reporte ratings during virtual reality. They also reported improve analgesia and affect improvements were maintained multiple therapy sessions.

N=54

= Standard Therapy

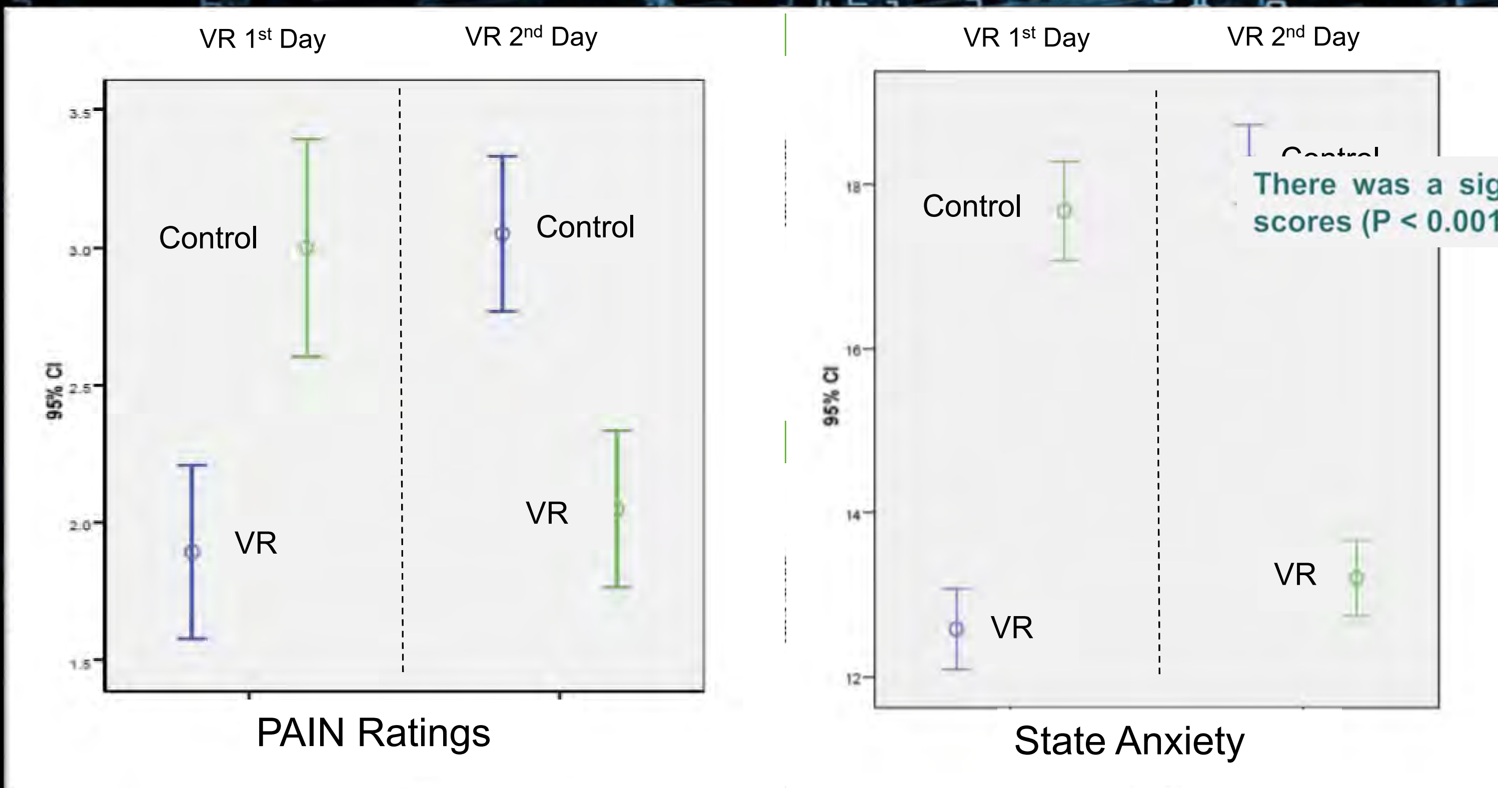
= VR w/Standard Therapy

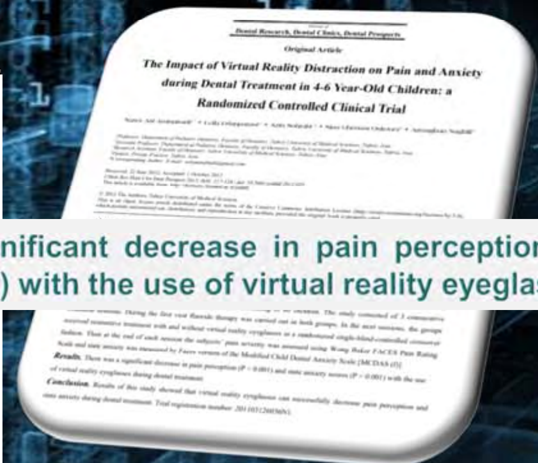
Schmitt, Y. S., Hoffman, H. G., Blough, D. K., Patterson, D. R., Jensen, M. P., Soltani, M., ... & Sharar, S. R. (2011). A randomized, controlled trial of immersive virtual reality analgesia, during physical therapy for pediatric burns. Burns, 37(1), 61-68.

DISTRACT

The Impact of Virtual Reality Distraction on Pain and Anxiety during Dental Treatment in 4-6 Year-Old Children: a Randomized Controlled Clinical Trial

VR Counterbalanced with Control over 2 Dental appointments





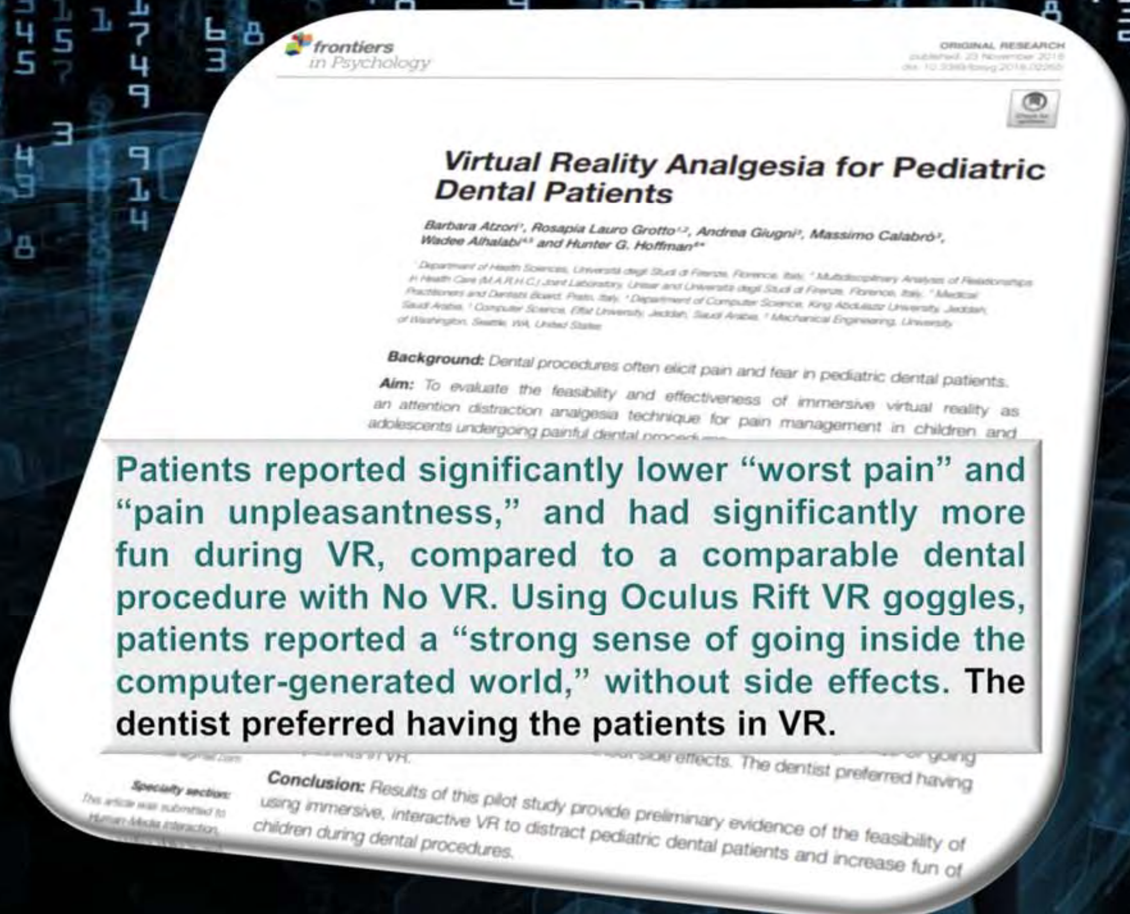
N=120; Aged 4-6

DISTRACT

Aminabadi, N. A., Erfanparast, L., Sohrabi, A., Oskouei, S. G., & Naghili, A. (2012). The impact of virtual reality distraction on pain and anxiety during dental treatment in 4-6 year-old children: a randomized controlled clinical trial. Journal of dental research, dental clinics, dental prospects, 6(4), 117.

Virtual Reality Analgesia for Pediatric Dental Patients

2018


frontiers in Psychology

ORIGINAL RESEARCH

Virtual Reality Analgesia for Pediatric Dental Patients

Barbara Atzori, Rosapia Lauro Grotto, Andrea Giugni, Massimo Calabrò, Wadee Alhalabi and Hunter G. Hoffman

Background: Dental procedures often elicit pain and fear in pediatric dental patients.

Aim: To evaluate the feasibility and effectiveness of immersive virtual reality as an attention distraction analgesia technique for pain management in children and adolescents undergoing painful dental procedures.

Conclusion: Results of this pilot study provide preliminary evidence of the feasibility of using immersive, interactive VR to distract pediatric dental patients and increase fun of children during dental procedures.

Patients reported significantly lower "worst pain" and "pain unpleasantness," and had significantly more fun during VR, compared to a comparable dental procedure with No VR. Using Oculus Rift VR goggles, patients reported a "strong sense of going inside the computer-generated world," without side effects. The dentist preferred having the patients in VR.

Atzori, B., Lauro Grotto, R., Giugni, A., Calabrò, M., Alhalabi, W., & Hoffman, H. G. (2018). Virtual reality analgesia for pediatric dental patients. Frontiers in psychology, 9, 2265.

DISTRACT

VR Pain Distraction for Children Undergoing Venipuncture

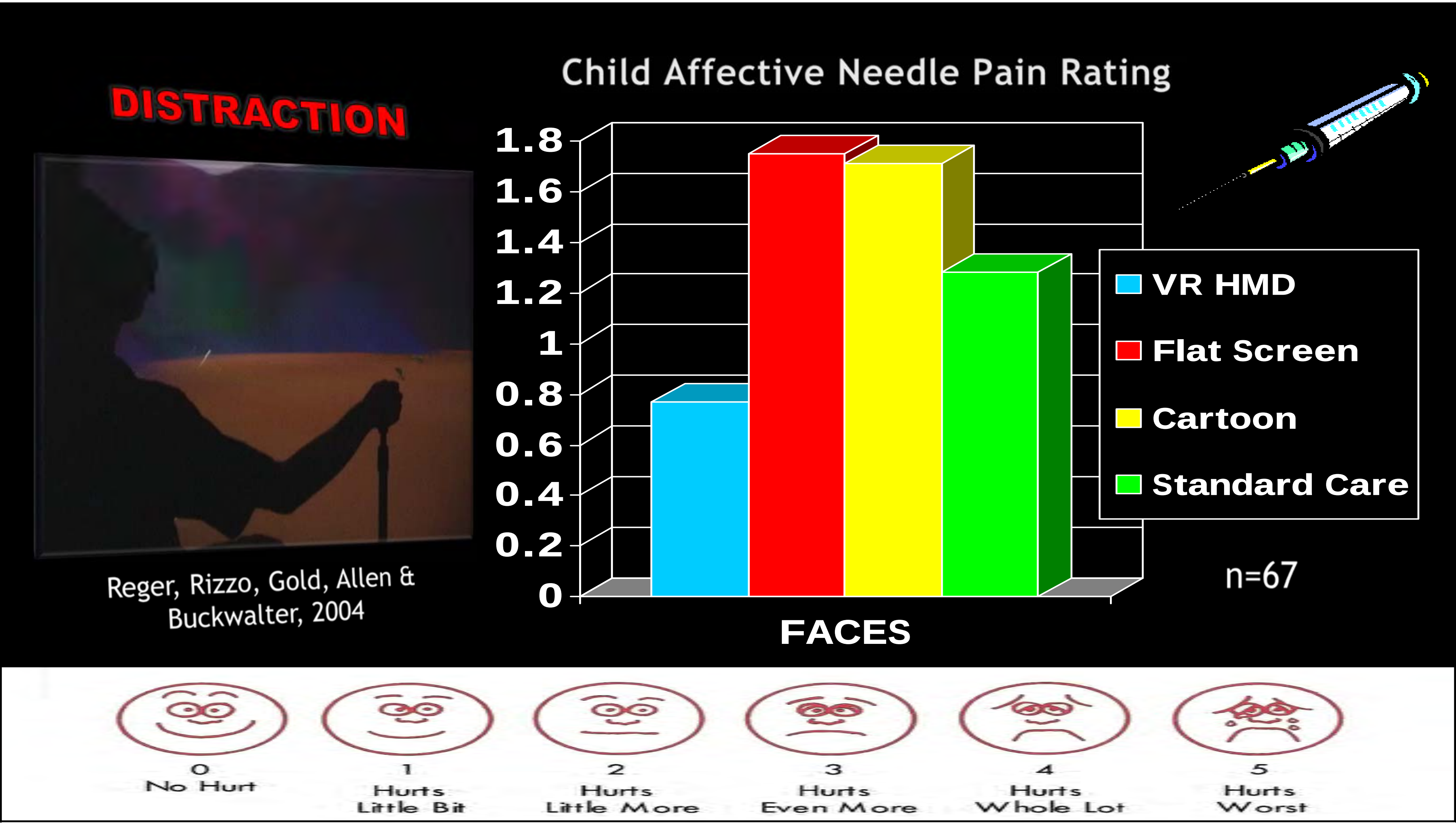
Reger, Rizzo, Gold, Allen & Buckwalter, 2004

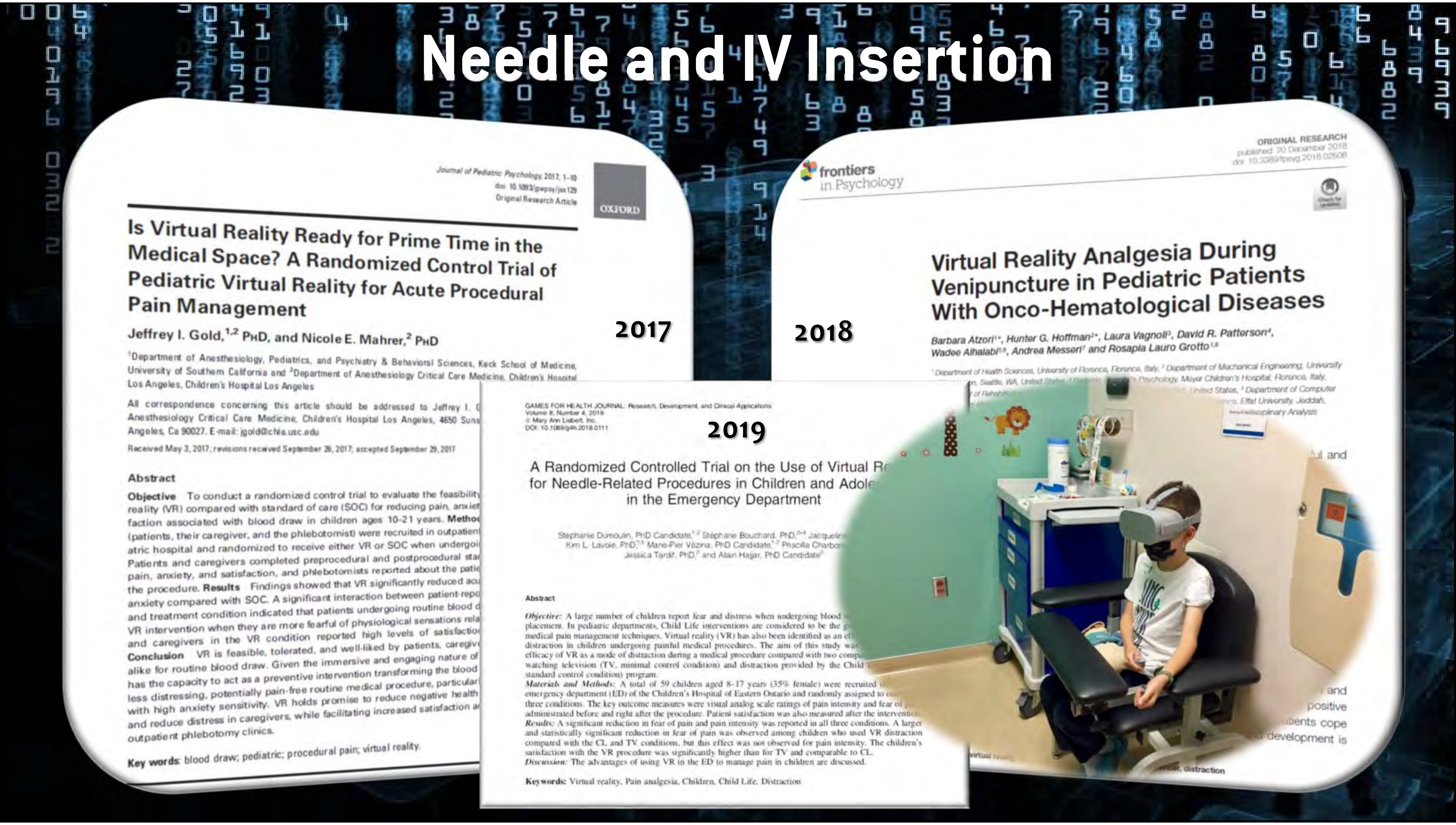
Between group comparison of 4 conditions:

- Standard Care + Visual Occlusion; n=18
- VR HMD w/Force Feedback Joystick; n=13
- VR Flatscreen w/Force Feedback Joystick; n=12
- Cartoon; n=14

Other Variables:* *Presence; Anxiety; Parental/Phlebotomist ratings; etc.

(n = 67)


DISTRACTION
Reger, Rizzo, Gold, Allen &
Buckwalter, 2004
Child Affective Needle Pain Rating
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
FACES
VR HMD
Flat Screen
Cartoon
Standard Care
n=67
0
No Hurt
1
Hurts
Little Bit
2
Hurts
Little More
3
Hurts
Even More
4
Hurts
Whole Lot
5
Hurts
Worst


Needle and IV Insertion
2017
Is Virtual Reality Ready for Prime Time in the Medical Space? A Randomized Control Trial of Pediatric Virtual Reality for Acute Procedural Pain Management
Jeffrey I. Gold, PhD, and Nicole E. Mahrer, PhD
2018
frontiers in Psychology
ORIGINAL RESEARCH
Virtual Reality Analgesia During Venipuncture in Pediatric Patients With Onco-Hematological Diseases
2019
GAMES FOR HEALTH JOURNAL: Research, Development, and Clinical Applications
A Randomized Controlled Trial on the Use of Virtual Re
for Needle-Related Procedures in Children and Adole
in the Emergency Department

What about Chronic Pain?

Contents lists available at ScienceDirect

International Journal of Biochemistry and Cell Biology

journal homepage:

Molecules in focus

Virtual Reality interventions for acute and chronic pain management

Naseem Ahmadpour, Hayden Randall, Harsham Choksi, Antony Gao, Christopher Vaughan, Philip Poronnik

ARTICLE INFO

ABSTRACT

"The evidence for impact of VR analgesia on chronic pain is under-investigated, compared to impacts on acute pain…more research is needed to support the long-term benefits of using VR for managing pain, <u>particularly for chronic pain</u>."

Stanford University

Chronic Pain Reduction by "tricking the brain"
Kim Bullock, Stanford University

DISCOMFORT REDUCTION

WHY "VIRTUAL DOCTOR" NEVER CAUGHT ON

Using Virtual Reality as a Distraction to Mitigate Chemotherapy Symptoms

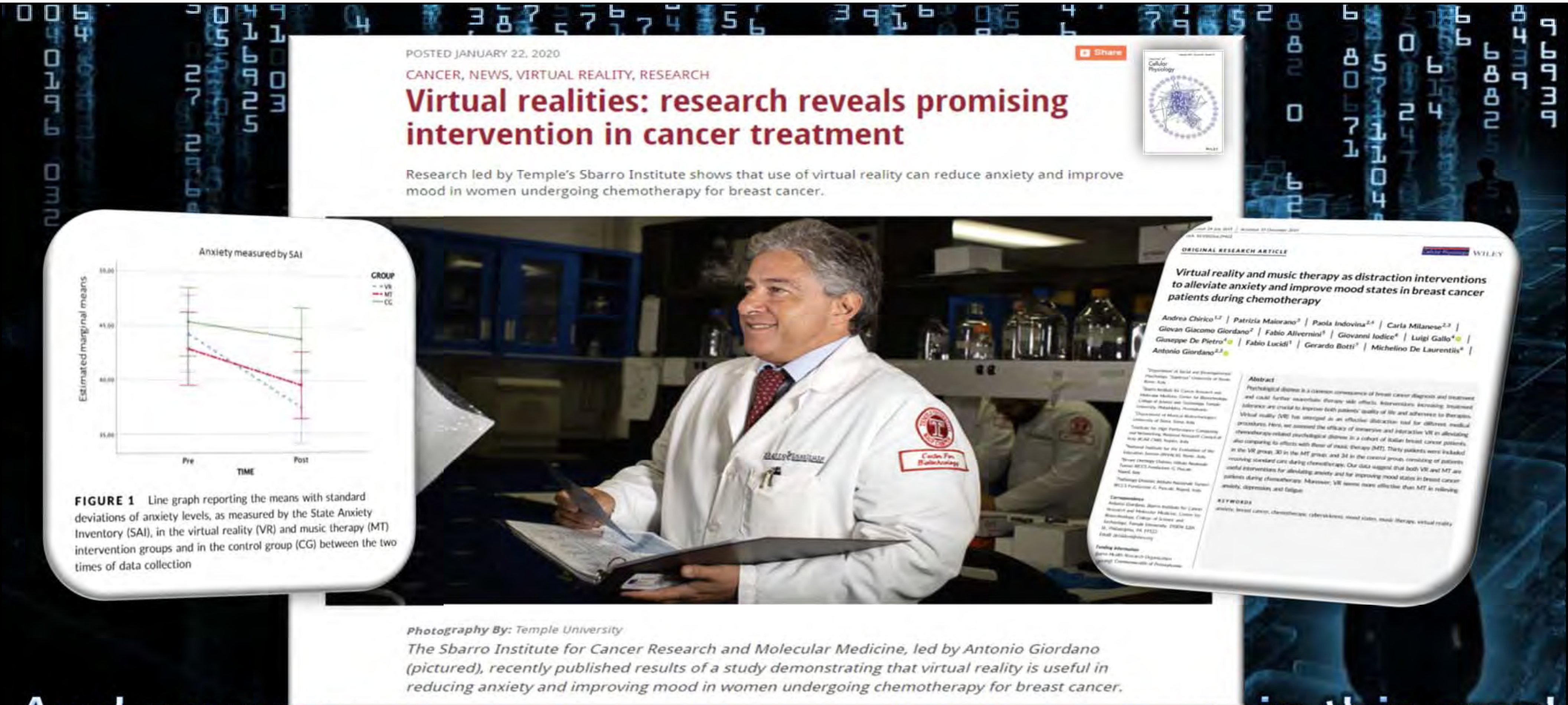
Susan M. Schneider, PhD, RN, AOCN
Duke University

2000-2004

Using Virtual Reality as a Distraction to Mitigate Chemotherapy Symptoms

Susan M. Schneider, PhD, RN, AOCN
Duke University

2000-2004



And new results (2020) confirm positive impact in this area!

VR and Music Therapy are useful interventions for alleviating anxiety and for improving mood states in breast cancer patients during chemotherapy. Moreover, VR seems more effective than Music Therapy in relieving anxiety, depression, and fatigue.

18Loop
https://www.18loop.org/
HOME
ABOUT US
OUR PROGRAM
VR for Kids with Cancer
DONATE
Are you better off overall with VR?
Answered: 7 Skipped: 0
Yes
No
Do you use Tripp at home or in ...
Answered: 7 Skipped: 0
I use Tripp at home.
I use Tripp in the hospital.
I use Tripp both at home...
18Loop/ACCO VR Survey
Are hospital stays better with T...
Answered: 7 Skipped: 0
Yes
No
18Loop/ACCO VR Survey
Does Tripp help with pain?
Answered: 7 Skipped: 0
Yes
No
18Loop/ACCO VR Survey
Does Tripp improve your mood?
Answered: 7 Skipped: 0
Yes
No
18Loop/ACCO VR Survey
childhood
CANCER ORGANIZATION

How far can we go in this area??

Mosso, et al. 2008

VR PAIN DISTRACTION REVIEW

(Hoffman et al., 2019)

Chapter 8
Virtual Reality Distraction to Help Control Acute Pain during Medical Procedures

Hunter G. Hoffman, Walter J. Meyer III, Sydney A. Drever, Maryam Soltani, Barbara Atzori, Rocio Herrero, Wadee Alhalabi, Todd L. Richards, Sam R. Sharar, Mark P. Jensen, and David R. Patterson

2019

Introduction

The Problem: Uncontrolled Pain

Uncontrolled pain is a widespread problem in medicine. Both military and civilian advisory committees have called for large improvements in pain control. The treatment of severely burn-injured patients is one of the most intensely painful processes

H. G. Hoffman
Human Photonics Lab, Department of Mechanical Engineering, University of Washington, Seattle, WA, USA

W. J. MeyerIII
University of Texas Medical Branch and Shriners Children's Hospital, Galveston, TX, USA

S. A. Drever · M. Soltani · M. P. Jensen · D. R. Patterson
Department of Rehabilitation Medicine, University of Washington, Seattle, WA, USA

B. Atzori
Department of Health Sciences, University of Florence, Florence, Italy

R. Herrero
University Jaume, Castellón, Spain

University of Washington, Seattle, USA

W. Alhalabi
Department of Computer Science, King Abdulaziz University, Jeddah, Saudi Arabia

Department of Computer Science, Effat University, Jeddah, Saudi Arabia

T. L. Richards
Department of Radiology, University of Washington, Seattle, WA, USA

S. R. Sharar
Department of Anesthesiology, University of Washington Harborview Medical Center, Seattle, WA, USA

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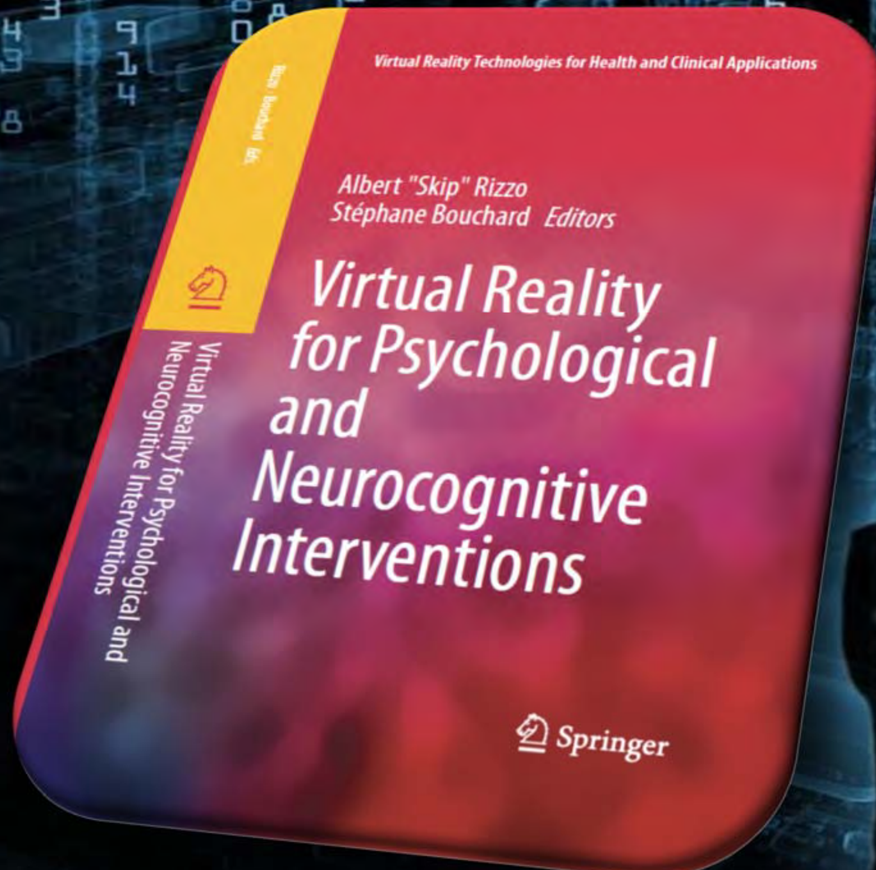
A. Rizzo, S. Bouchard (eds.), *Virtual Reality for Psychological and Neurocognitive Interventions*, Virtual Reality Technologies for Health and Clinical Applications, https://doi.org/10.1007/978-1-4939-9482-3_8



Request copy at: rizzo@ict.usc.edu


4. REHABILITATE BRAIN OR SPINAL CORD INJURY
4

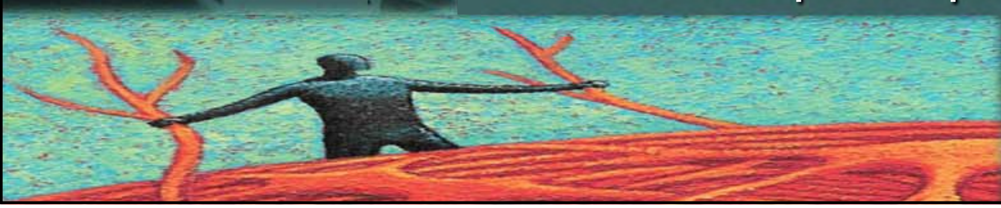
Traditional Physical Therapy

Virtual Reality Physical Therapy

Theoretical Basis: *Physical/Cognitive Assessment and Rehabilitation*

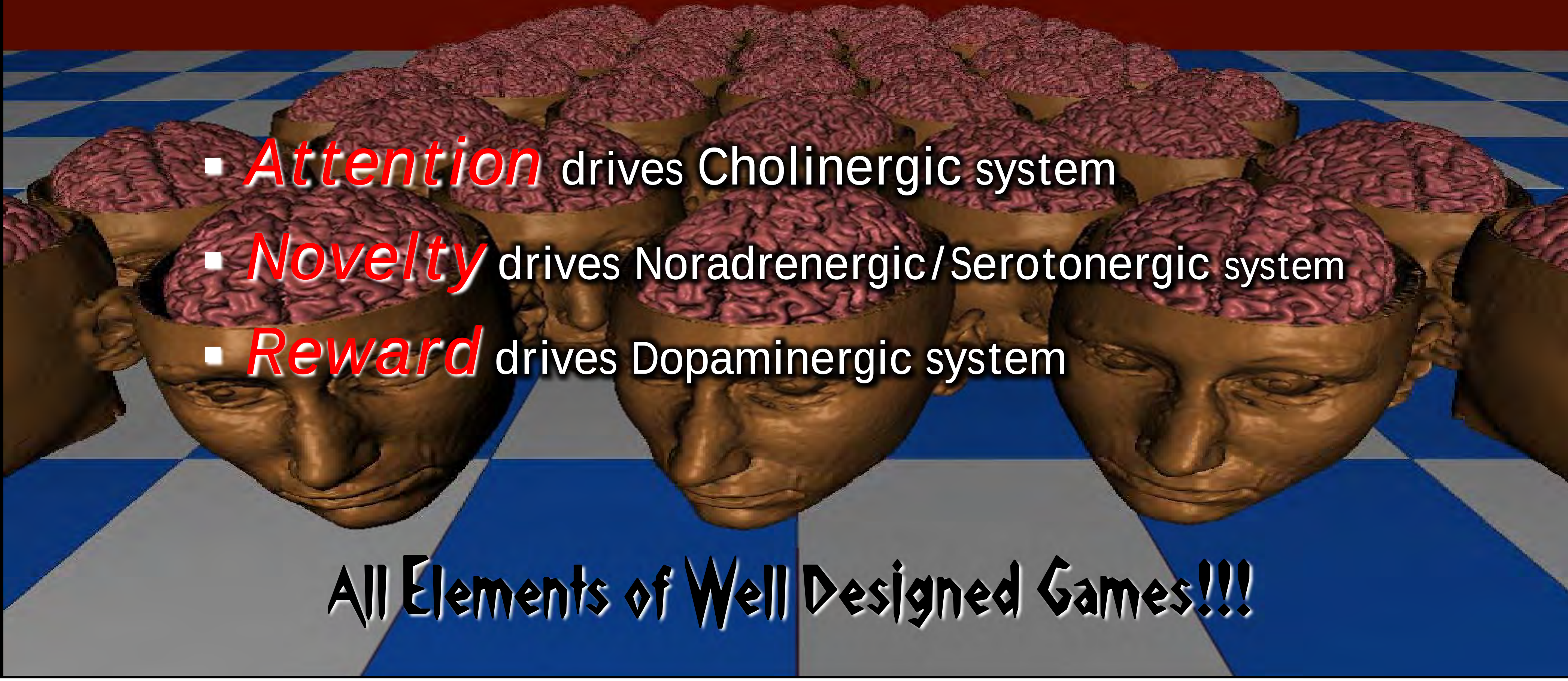
Rehabilitation Tasks Must:

- focus on specific targets derived from **data-driven assessment** to direct treatment
- be **adjustable in terms of difficulty level** from something simple for the patient to accomplish, to a level nearing normal performance
- be administered **repetitively** and **hierarchically**
- be **quantifiable** in order to assess progress
- provide the client with **strategic feedback** as to the outcome of performance
- have some **relevance** to real world function
- **motivate participation!**



Neuroscience Rationale

(based on Merzenich's Model on drivers for Neuroplasticity)



- *Attention* drives Cholinergic system
- *Novelty* drives Noradrenergic/Serotonergic system
- *Reward* drives Dopaminergic system

All Elements of Well Designed Games!!!

And, Games Can Enhance Motivation!!!

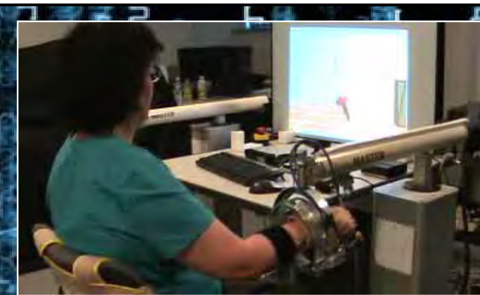
Robotically Facilitated Training of the Hemiplegic Upper Extremity as an Integrated Functional Unit in Virtual Environments

Alma Merians & Gerard Fluet
University of Medicine and Dentistry of New Jersey
Sergei Adamovich, Qinyin Qiu & Ian Lafond
New Jersey Institute of Technology

2009


Clinical Outcomes

Functional Improvement



Subjects

- Mean age = 58
- 7 male 4 female
- Mean - 6 yrs. post stroke (9 mos-15 yrs)
- 6 right hemiplegia, 5 left hemiplegia
- All cortical - ischemic strokes
- 6 Months Post CVA

Training = 20 Hours over 2 Weeks (8-10 sessions)

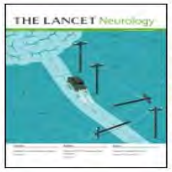
Four game simulations that combined arm transport and hand manipulation

Test	Percent Change (SD)	P value
Jebsen Test of Hand Function	28% (15)	P=.03*
Wolf Motor Function Test	25% (11)	P=.000025*
9 hole peg test	19% (30)	P=.08
Box and Blocks Test	12% (10)	P=.02*

Exclusion Criteria: severe aphasia, hemispatial neglect, upper extremity botox within 3 months

Merians, Adamovich, Qiu, Lafond & Fluet, 2009

2009



THE LANCET Neurology

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Articles

Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomised trial

Verena Klamroth-Marganska, Javier Blanco, Katrin Campen, Armin Curt, Volker Dietz, Thierry Ettlin, Morena Felder, Bernd Fellinghauer, Marco Guidali, Anja Kollmar, Andreas Luft, Tobias Nef, Corina Schuster-Amft, Werner Stahel, Robert Riener

Lancet Neurol 2014; 13: 159–66

24 Sessions: Robot Assisted VR Therapy Improved outcomes over USUAL CARE

Summary

Background Arm hemiparesis secondary to stroke is common and disabling. We aimed to assess whether robotic

impairment for more than 6 months and moderate-to-severe arm paresis after a cerebrovascular accident who met our eligibility criteria from four centres in Switzerland. Eligible patients were randomly assigned (1:1) to receive robotic or conventional therapy using a centre-stratified randomisation procedure. For both groups, therapy was given for at least 45 min three times a week for 8 weeks (total 24 sessions). The primary outcome was change in score on the arm (upper extremity) section of the Fugl-Meyer assessment (FMA-UE). Assessors tested patients immediately before therapy, after 4 weeks of therapy, at the end of therapy, and 16 weeks and 34 weeks after start of therapy. Assessors were masked to treatment allocation, but patients, therapists, and data analysts were unmasked. Analyses were by modified intention to treat. This study is registered with ClinicalTrials.gov, number NCT00719433.

Findings Between May 4, 2009, and Sept 3, 2012, 143 individuals were tested for eligibility, of whom 77 were eligible and agreed to participate. 38 patients assigned to robotic therapy and 35 assigned to conventional therapy were included in analyses. Patients assigned to robotic therapy had significantly greater improvements in motor function in the affected arm over the course of the study as measured by FMA-UE than did those assigned to conventional therapy (F=4·1, p=0·041; mean difference in score 0·78 points, 95% CI 0·03–1·53). No serious adverse events related to the study occurred.

Interpretation Neurorehabilitation therapy including task-oriented training with an exoskeleton robot can enhance improvement of motor function in a chronically impaired paretic arm after stroke more effectively than conventional therapy. However, the absolute difference between effects of robotic and conventional therapy in our study was small and of weak significance, which leaves the clinical relevance in question.

Sensory-Motor Systems Lab, Institute of Robotics and Intelligent Systems, Department of Health Sciences and Technology (V Klamroth-Marganska MD, M Guidali PhD, A Kollmar, Prof R Riener PhD), and Seminar for Statistics (B Fellinghauer PhD, W Stahel PhD), ETH Zurich, Zurich, Switzerland; Spinal Cord Injury Center, University Hospital Balgrist (V Klamroth-Marganska, Prof A Curt MD, Prof V Dietz MD, M Guidali, A Kollmar, Prof R Riener), and Clinical Neurorehabilitation, Department of Neurology (Prof A Luft MD), University of Zurich, Zurich, S

Zürcher Höhenk

Switzerland

(J Blanco MD, M F

2015

USC ICT Rehabilitation Lab Novel Interface Projects

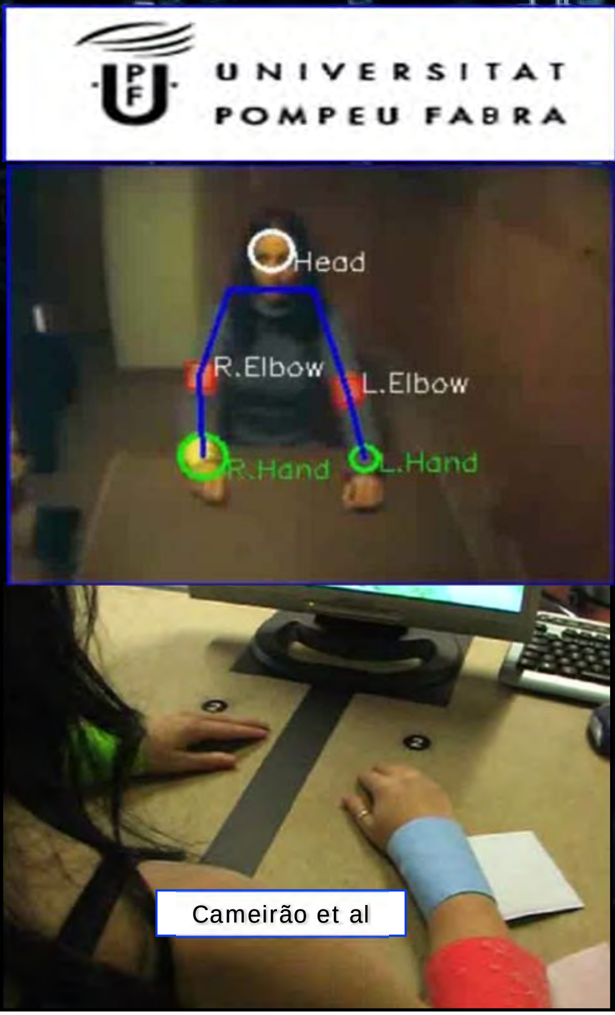
Bi-Manual Coordination

Digital Spirometer Breathing Game

Pinch and Grasp training

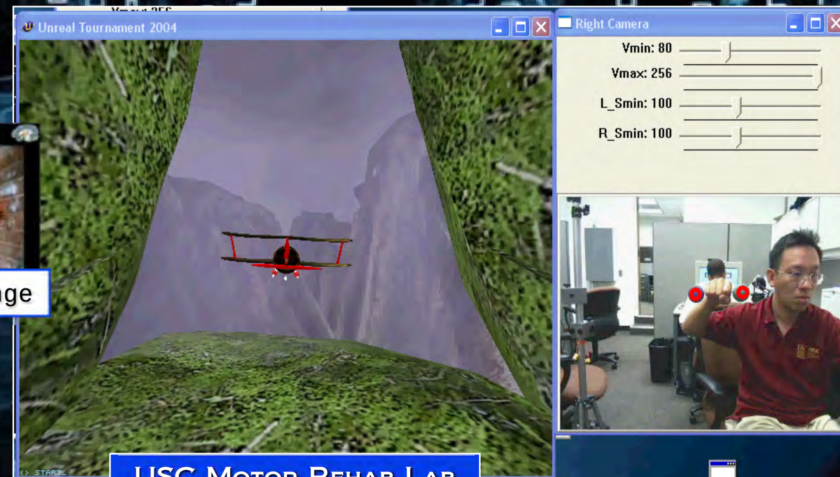
Supination/Pronation/Reaching

Various Labs began developing Infrared & Webcam-based Tracking Options…2005-2012



Cameirão et al

Rizzo, Yeh, & Lange



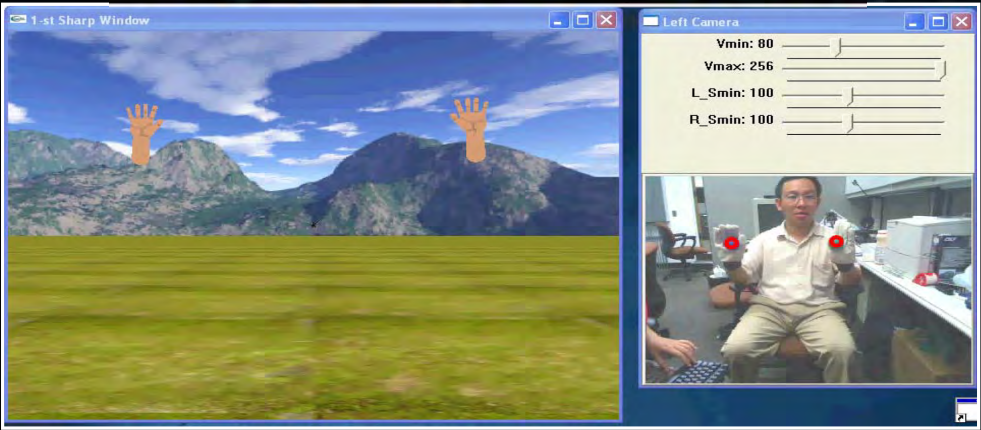
USC Motor Rehab Lab

Alcaniz et al

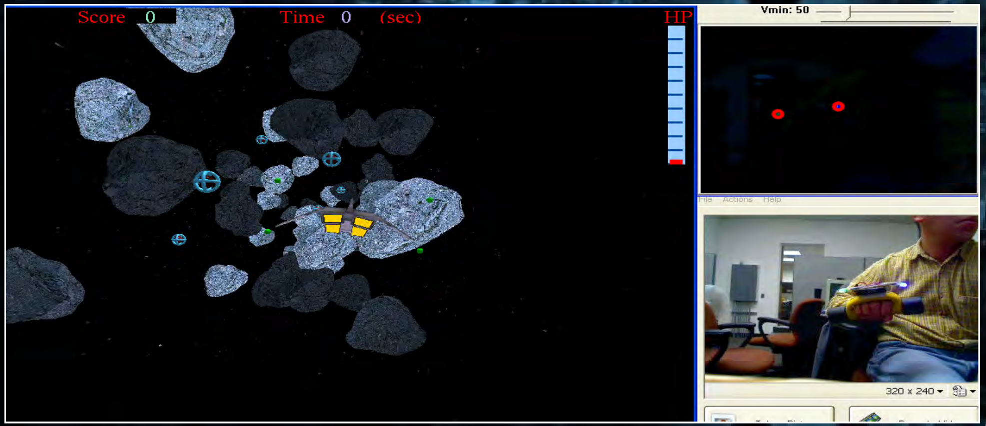
USC ICT Rehabilitation Lab WebCam Projects

Balance Training

Web-Cam tracked UE Range of Motion



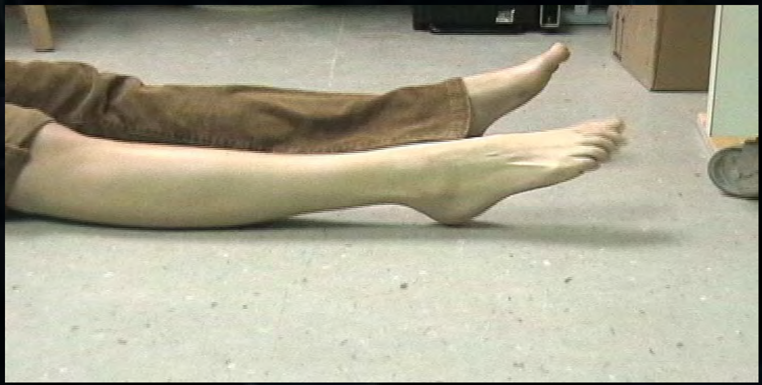
Supination/Pronation/Reaching



Feasibility, Motivation and Selective Motor Control: Virtual Reality Compared to Conventional Home Exercise in Children with Cerebral Palsy

Carolyn Bryanton[1], Marie Brien[2], Jennifer McLean[2], Anna McCormick[2], Heidi Sveistrup[1]

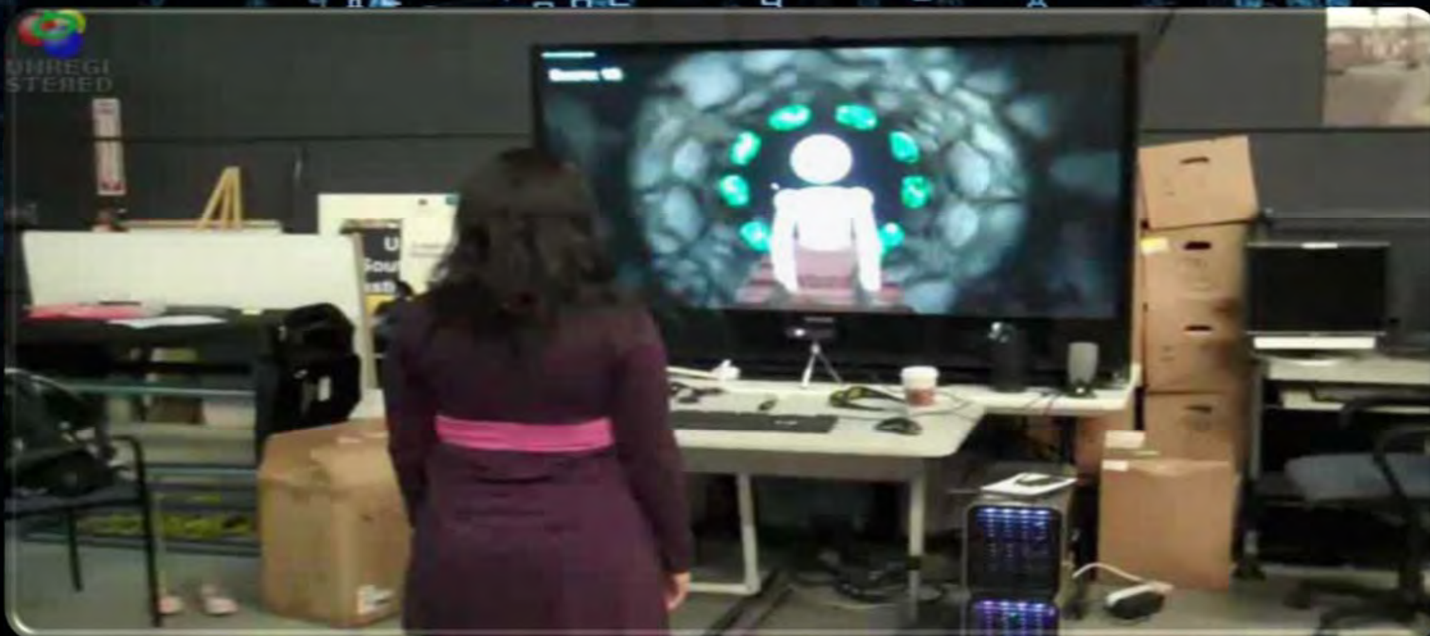
Children generate a greater range of ankle dorsiflexion, demonstrate better control of active ankle dorsiflexion movement, and report greater interest in doing the same exercise when delivered through a virtual reality system than as a stand-alone exercise. The next series of experiments will characterize the muscle activity generated during the two exercise modes as well as determine retention and transfer of effects following an intervention trial.



2006

MedVRlab

Kinect Motion Tracking Interface Project



Jewel Mine Upper Extremity Range of Motion Early Prototype

USC Institute for Creative Technologies

(Lange, Koenig, Rizzo, et al, 2010)


MedVRlab
MYSTIC ISLE
A REHABILITATION ADVENTURE
USC Institute for Creative Technologies
(Lange, Koenig, Rizzo, et al, 2013)


MedVRlab
MYSTIC ISLE
THE BEACH LANDING
USC Institute for Creative Technologies
This is the starting point of the adventure
(Lange, Koenig, Rizzo, et al, 2013)


MedVRlab
MYSTIC ISLE
THE FOREST ROAD
Venture if you dare!
USC Institute for Creative Technologies
(Lange, Koenig, Rizzo, et al, 2013)

Venture if you dare!

USC Institute for Creative Technologies

(Lange, Koenig, Rizzo, et al, 2013)

Oculus-Leap Motion Sensor for Hand Tracking

(Rizzo, Liew, Chang, Schiavi, Gechter, et al)

And now with the Oculus Quest!!!

http://tandfonline.com/ibij
ISSN: 0269-9052 (print), 1362-301X (electronic)

BRAIN INJURY

Brain Inj, 2016; 30(7): 855–863

DOI: 10.3109/02699052.2016.1144146

Taylor & Francis
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REVIEW ARTICLE

Virtual reality gaming in the rehabilitation of the upper extremities post-stroke

Michael Yates [1], Arpad Kelemen [1], & Cecilia Sik Lanyi [2]

[1]School of Nursing, University of Maryland, Baltimore, MD, USA and [2]Department of Electrical Engineering and Information Systems, University of Pannonia, Veszprem, Hungary

Abstract

Background: Occurrences of strokes often result in unilateral upper limb dysfunction. Dysfunctions of this nature frequently persist and can present chronic limitations to activities of daily living.
Methods: Research into applying virtual reality gaming systems to provide rehabilitation

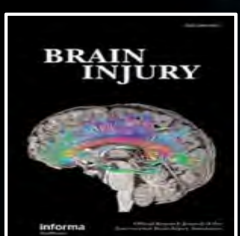
Results: The literature supports the use of virtual reality gaming rehab therapy as equivalent to traditional therapies or as successful augmentation to those therapies. While some degree of rigor was displayed in the literature, small sample sizes, variation in study lengths and therapy durations and unequal controls reduce generalizability and comparability.
Conclusions: Future studies should incorporate larger sample sizes and post-intervention follow-up measures.

Keywords

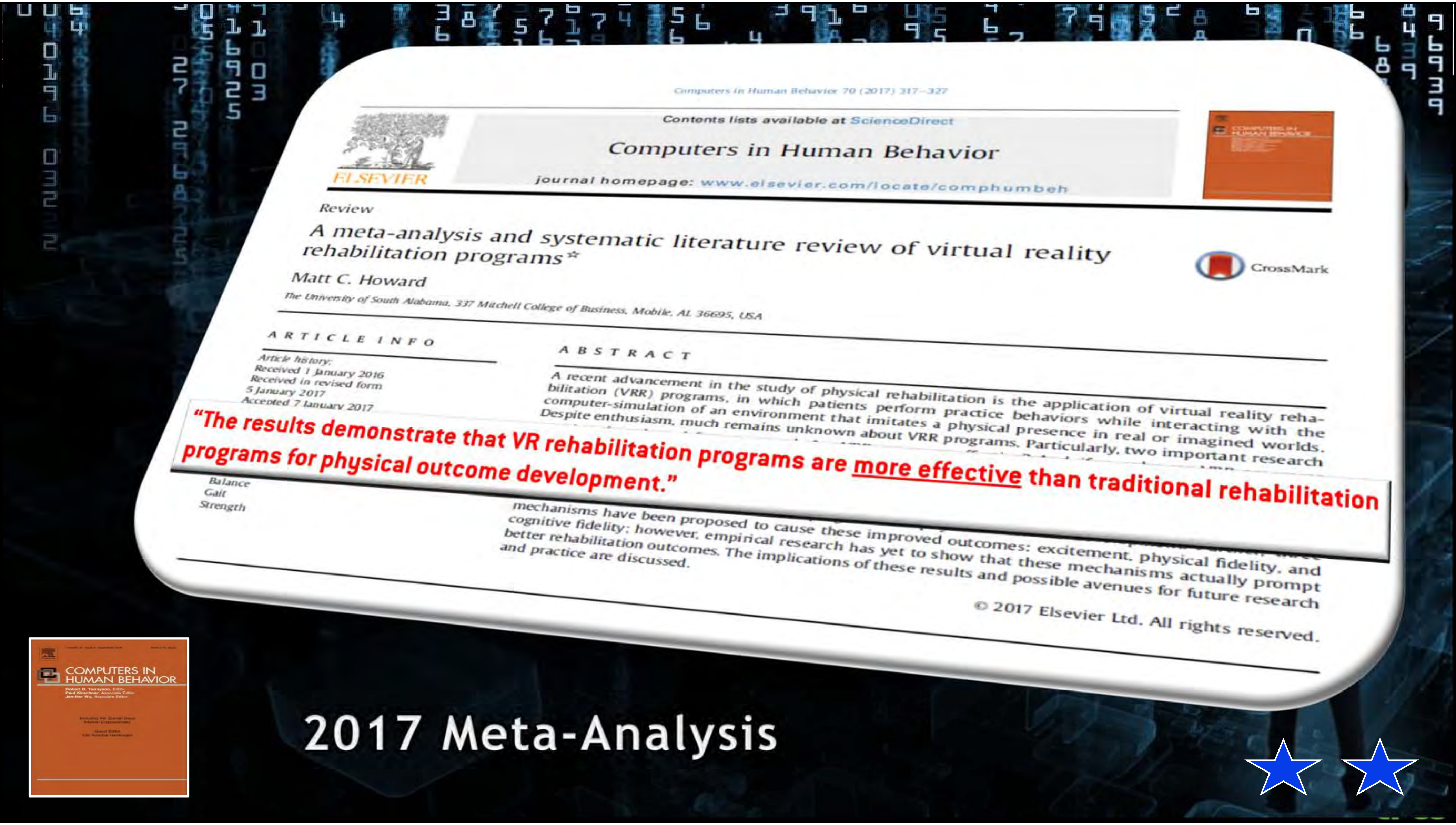
Gamification, commercial game system, Nintendo Wii, Microsoft Xbox Kinect, Sony PlayStation EyeToy, head-mounted display, interactive rehabilitation

Published online 28 March 2016

"The literature supports the use of virtual reality gaming rehab therapy as equivalent to traditional therapies or as successful augmentation to those therapies."



2016 Review



Computers in Human Behavior 70 (2017) 317–327

Contents lists available at ScienceDirect

Computers in Human Behavior

journal homepage: www.elsevier.com/locate/comphumbeh

ELSEVIER

Review

A meta-analysis and systematic literature review of virtual reality rehabilitation programs☆

CrossMark

Matt C. Howard

The University of South Alabama, 337 Mitchell College of Business, Mobile, AL 36695, USA

ARTICLE INFO

Article history:
Received 1 January 2016
Received in revised form
5 January 2017
Accepted 7 January 2017

Balance
Gait
Strength

ABSTRACT

A recent advancement in the study of physical rehabilitation is the application of virtual reality rehabilitation (VRR) programs, in which patients perform practice behaviors while interacting with the computer-simulation of an environment that imitates a physical presence in real or imagined worlds. Despite enthusiasm, much remains unknown about VRR programs. Particularly, two important research

mechanisms have been proposed to cause these improved outcomes: excitement, physical fidelity, and cognitive fidelity; however, empirical research has yet to show that these mechanisms actually prompt better rehabilitation outcomes. The implications of these results and possible avenues for future research and practice are discussed.

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BRAIN INJURY
https://doi.org/10.1080/02699052.2020.1725126

Taylor & Francis
Taylor & Francis Group

Check for updates

Virtual reality therapy for upper limb rehabilitation in patients with stroke: a meta-analysis of randomized clinical trials

Destaw B. Mekbib[a], Jiawei Han[b], Li Zhang[c], Shan Fang[c], Hongjie Jiang[b], Junming Zhu[b], Anna W. Roe[a], and Dongrong Xu[d]

[a]Zhejiang University Interdisciplinary Institute of Neuroscience and Technology (ZIINT), College of Biomedical Engineering and Instrument Science, Zhejiang University, Hangzhou, China; [b]The Second Affiliated Hospital, Zhejiang University School of Medicine, Zhejiang University, Hangzhou, China; [c]Department of Rehabilitation Medicine, Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Hangzhou, China; [d]Molecular Imaging and Neuropathology Division, Department of Psychiatry, Columbia University & New York State Psychiatric Institute, NY, USA

ABSTRACT

Background: Stroke is a major cause of life-long disability in adults, associated with poor quality of life. Virtual reality (VR)-based therapy systems are known to be helpful in improving motor functions following stroke, but recent clinical findings have not been included in the previous publications of meta-analysis studies.

Aims: This meta-analysis was based on the available literature to evaluate the therapeutic potential of VR as compared to dose-matched conventional therapies (CT) in patients with stroke.

Methods: We retrieved relevant articles in EMBASE, MEDLINE, PubMed, and Web of Science published

Conclusion: VR appears to be a promising therapeutic technology for UL motor rehabilitation in patients with stroke.

ARTICLE HISTORY
Received 28 April 2019
Revised 19 September 2019
Accepted 26 November 2019

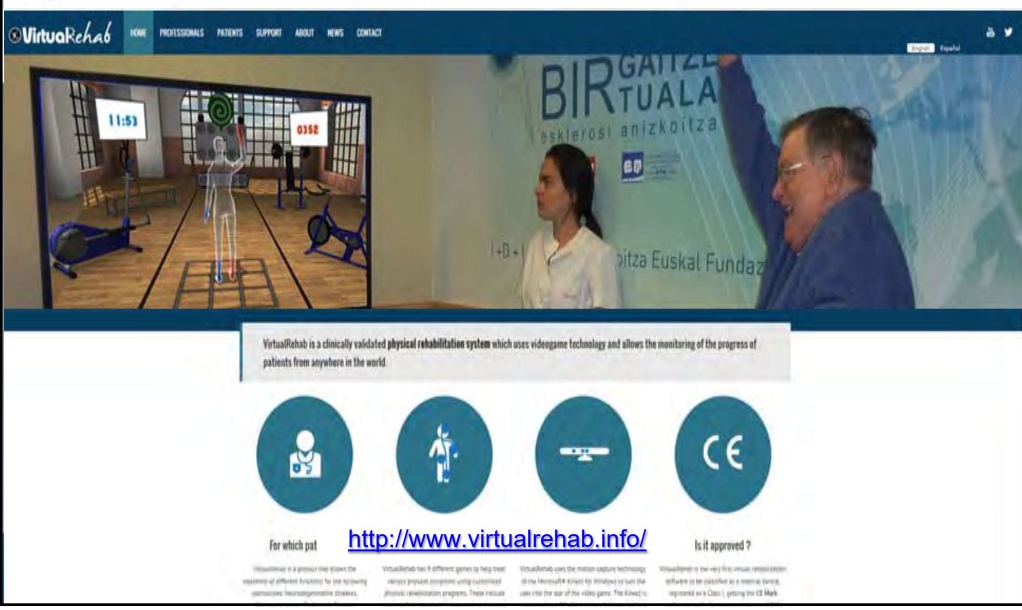
KEYWORDS
Stroke; stroke rehabilitation; virtual reality therapy; upper limb

"A total of 27 studies met the inclusion criteria. The analysis indicated that the VR group showed statistically significant improvement in the recovery of UL function, activity, and participation versus the control group. VR appears to be a promising therapeutic technology for UL motor rehabilitation in patients with stroke."

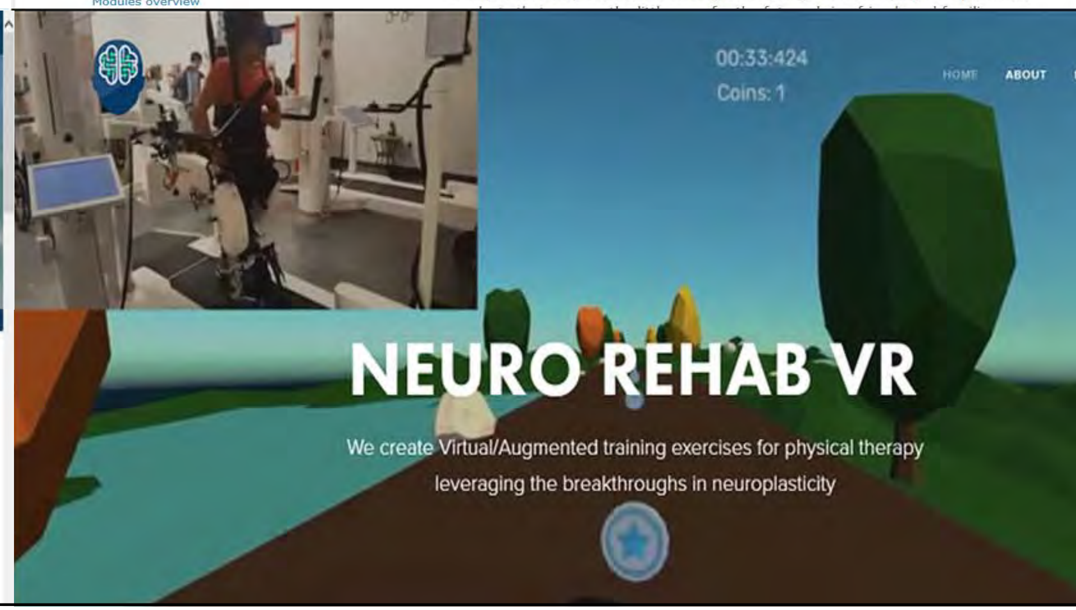
2020 Meta-Analysis

Tyromotion Introduces Virtual Reality to Robotic Therapy to Facilitate Stroke Recovery
BY: FG Team 15 April 2016
Images: TYROMOTION

Virtual Reality
Kinect Rehabilitation
Home
Articles
Our products
Download
Documents
Ordering
Contact
SeeMe system
Home rehabilitation
Home rehabilitation
Rehabilitation doesn't have to be complicated or take a lot of time. Usually (please ask your therapist or doctor) any physical activity will influence you in very positive way – especially when you can spend this time having fun with your family.
Home » Our products »
http://www.virtual-reality-rehabilitation.com/products/home-rehabilitation/is-it-possible
Our products
SeeMe system
What is SeeMe?
Key features
Video presentation
Modules overview
Is home rehabilitation possible?
Rehabilitation doesn't have to be complicated or take a lot of time. Usually (please ask your therapist or doctor) any physical activity will influence you in very positive way – especially when you can spend this time having fun with your family. That's why Brontes Processing is designing and developing family oriented



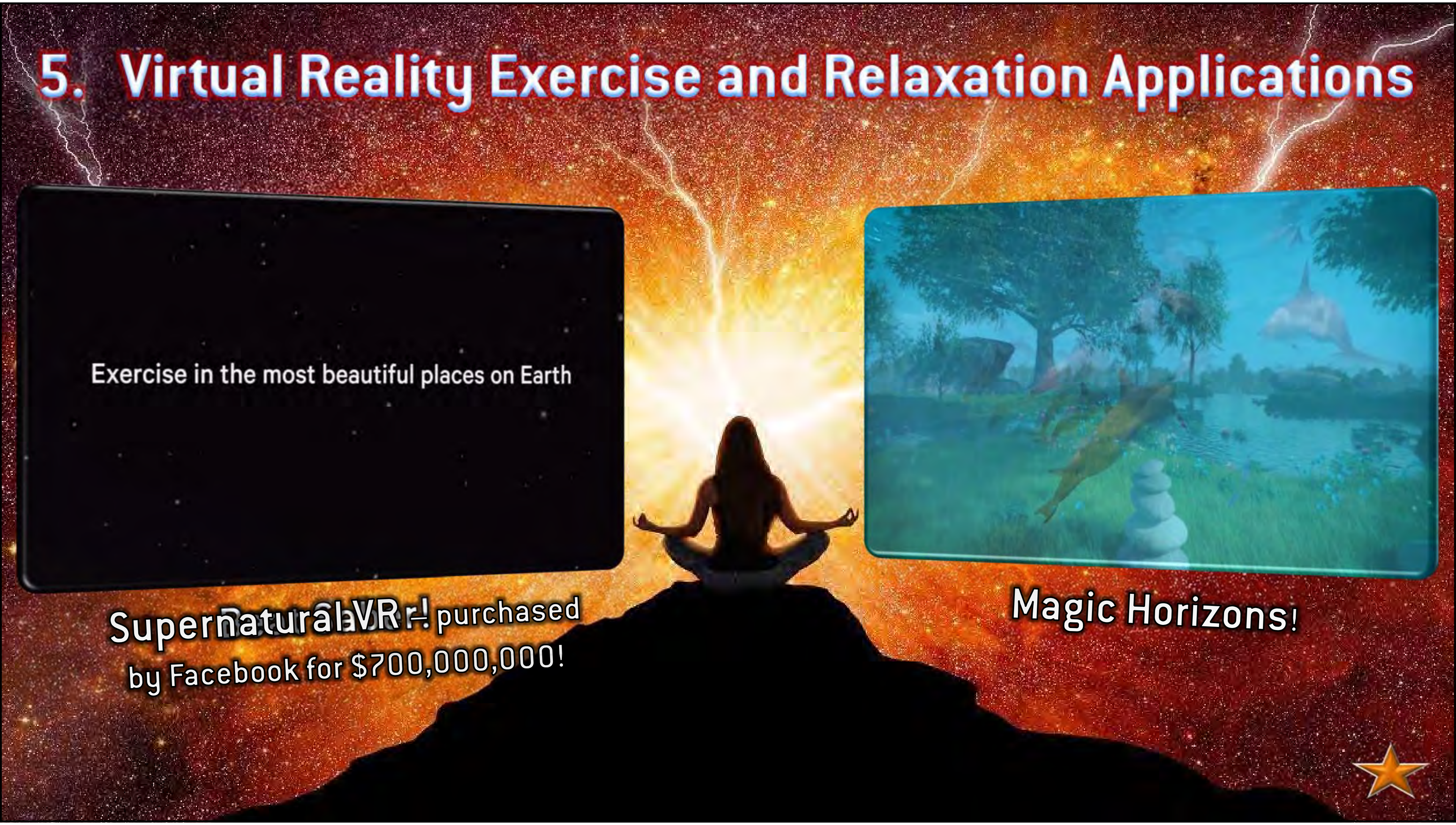
VirtuaRehab
HOME
PROFESSIONALS
PATIENTS
SUPPORT
ABOUT
NEWS
CONTACT
VirtualRehab is a clinically validated physical rehabilitation system which uses videogame technology and allows the monitoring of the progress of patients from anywhere in the world
For which pat
http://www.virtualrehab.info/
Is it approved ?

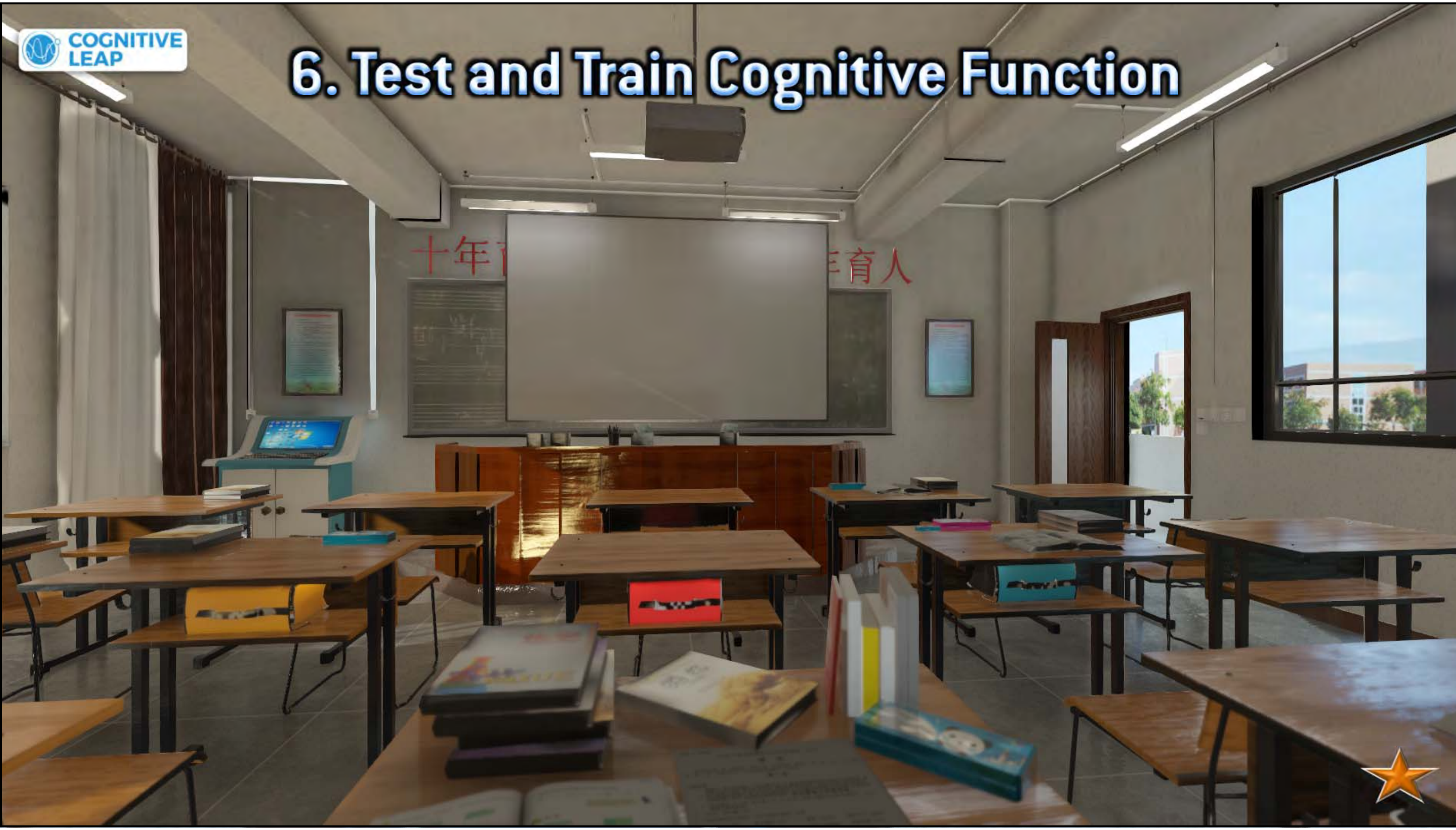


00:33:424
Coins: 1
HOME
ABOUT
NEURO REHAB VR
We create Virtual/Augmented training exercises for physical therapy leveraging the breakthroughs in neuroplasticity


2020-Present
REAL
REAL TABLET with TherapyView™ app
Physical Assessment/Rehabilitation
HEALTH
BUILDING A BETTER BAY AREA
THE POWER OF HEALING THROUGH TECH
ABC7 NEWS
abc 7
5:26
63°
BALANCE
MOTOR SKILLS
REAL™ Immersive System
Making Rehab Fun
Penumbra
Cognitive Assessment/Rehabilitation


2020-Present
REAL
I-Series
WORLD TRAVELER
REAL TABLET with TherapyView™ app
My Mom Revisits Rome!
REAL HEADSET
REAL CASE
ust Order Separately:
REAL Sensor Bands
REAL™ Immersive System
Making Rehab Fun
Penumbra


5. Virtual Reality Exercise and Relaxation Applications
Exercise in the most beautiful places on Earth
SupernaturalVR – purchased by Facebook for $700,000,000!
Magic Horizons!

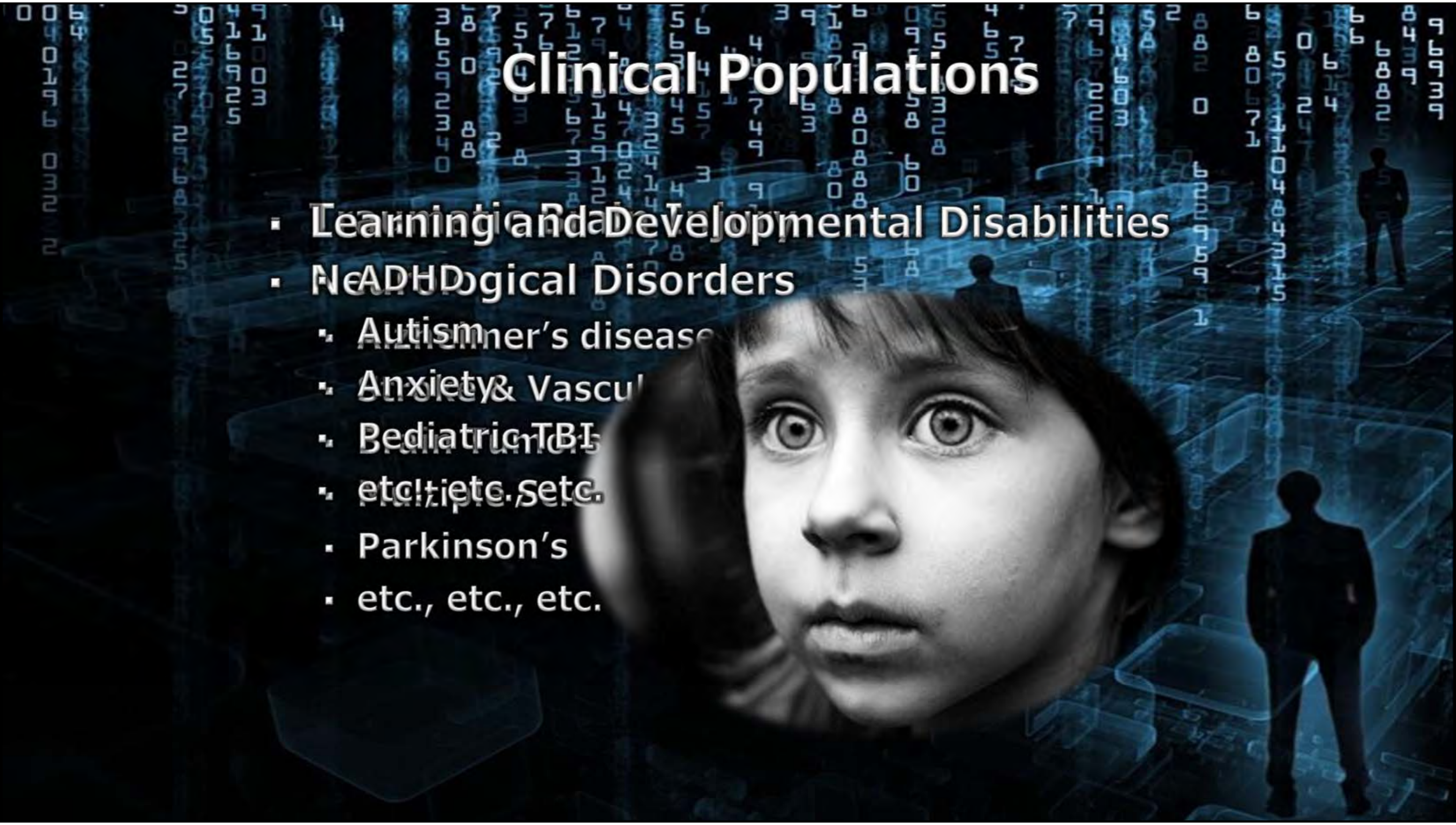

COGNITIVE LEAP
6. Test and Train Cognitive Function
十年
育人

Neuropsychological Methods

Neuropsychological Assessment

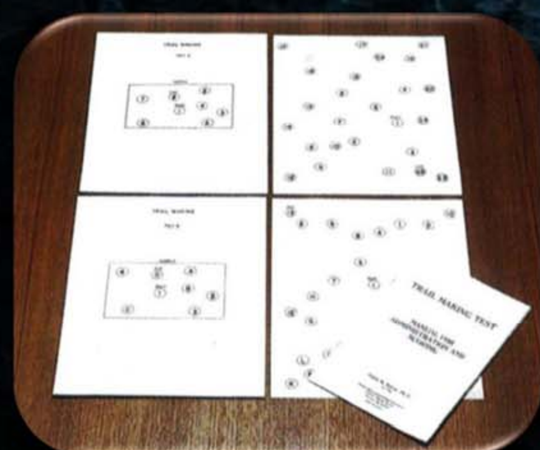
Cognitive Training
and Rehabilitation

Scientific study of cognitive
& functional processes


Clinical Populations
Learning and Developmental Disabilities
ADHD
Autism
Anxiety
Pediatric TBI
etc., etc., etc.
Neurological Disorders
Alzheimer's disease
& Vascul
Parkinson's
etc., etc., etc.

Traditional Assessment Methods

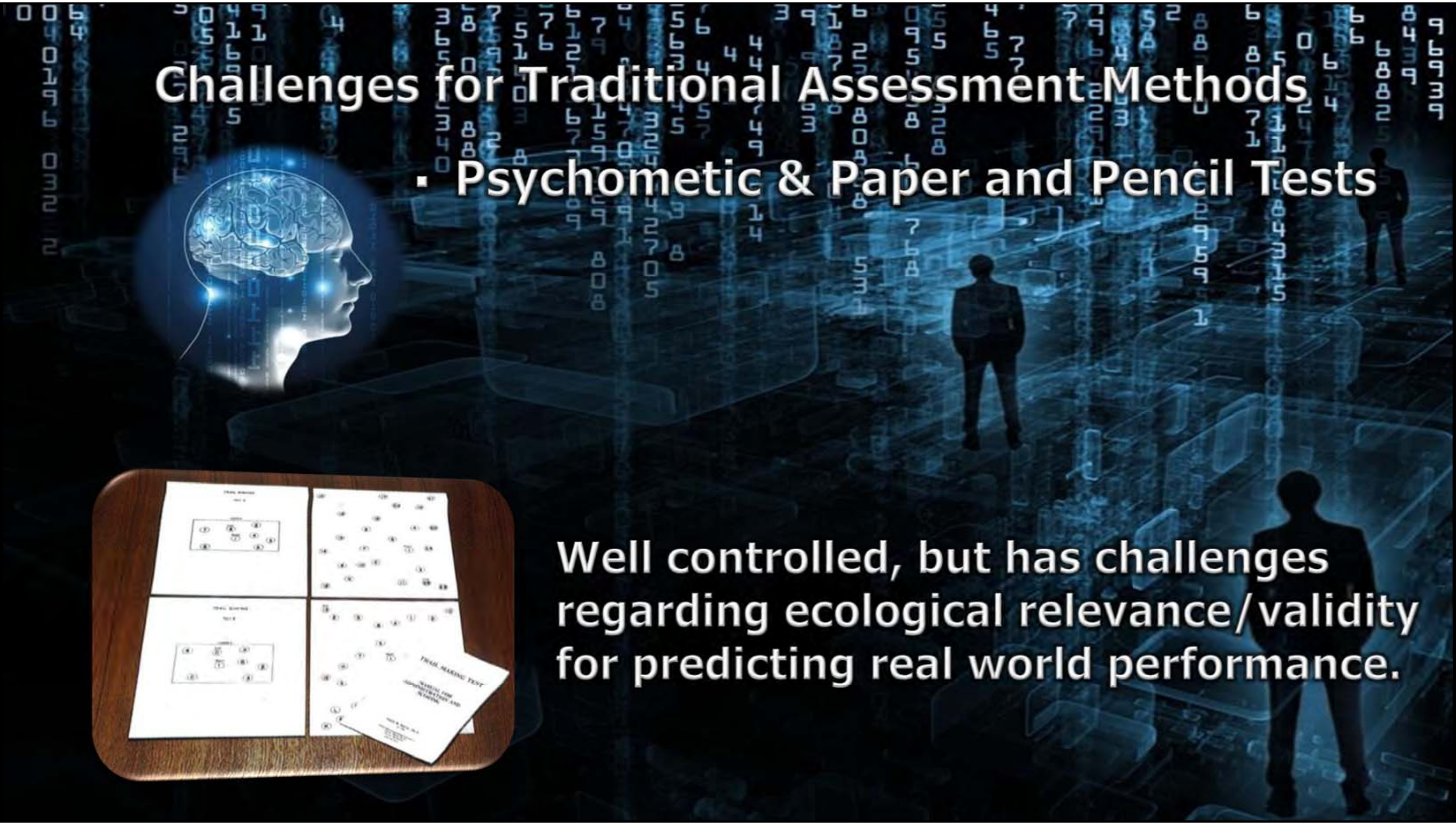
- History Taking
- Behavioral Rating Scales
- Psychometic & Paper and Pencil Tests
- Computerized Tests



Challenges for Traditional Assessment Methods

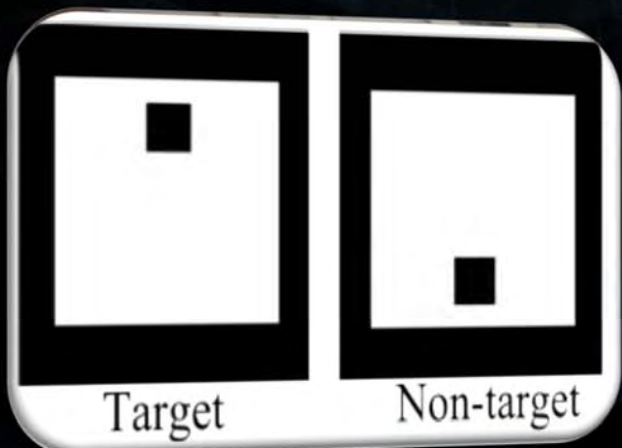
- History Taking
- Behavioral Rating Scales

Necessary, but limited by the bias & subjective impressions of the person reporting and doing the ratings!


Challenges for Traditional Assessment Methods
▪ Psychometic & Paper and Pencil Tests
Well controlled, but has challenges regarding ecological relevance/validity for predicting real world performance.

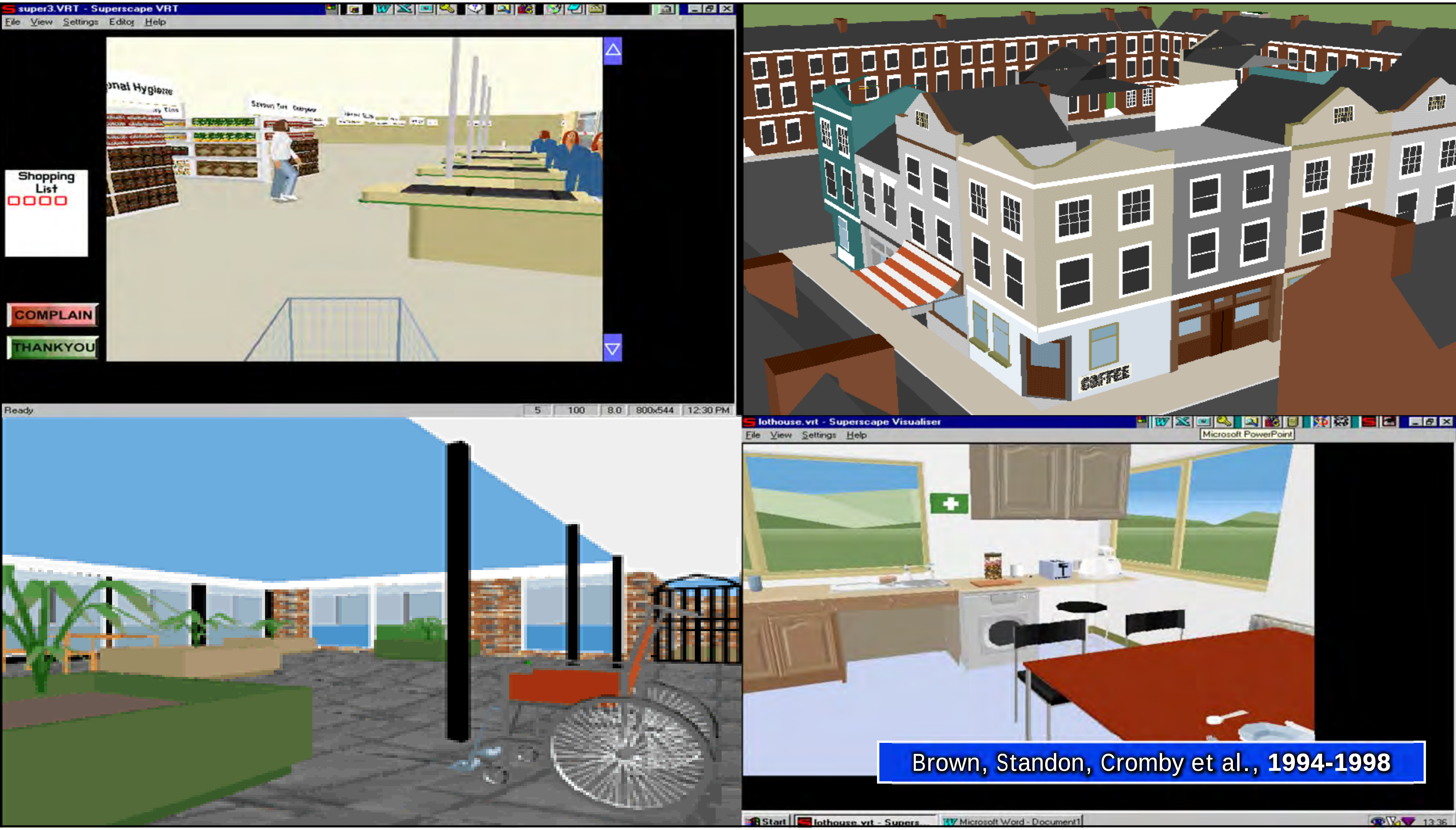
Challenges for Traditional Assessment Methods

- Computerized Tests



Also well controlled, but has challenges regarding ecological relevance/validity for predicting real world performance.


Remember—Simulator Metaphor



Brown, Standon, Cromby et al., **1994-1998**

1995 VR Conference Proceedings

1995 VR Conference Proceedings

Go to previous article
Go to next article
Return to 1995 VR Table of Contents

CAN STUDENTS WITH DEVELOPMENTAL DISABILITY USE VIRTUAL REALITY TO LEARN SKILLS WHICH WILL TRANSFER TO THE REAL WORLD?

Standen, P.J. & Cromby, J.J.

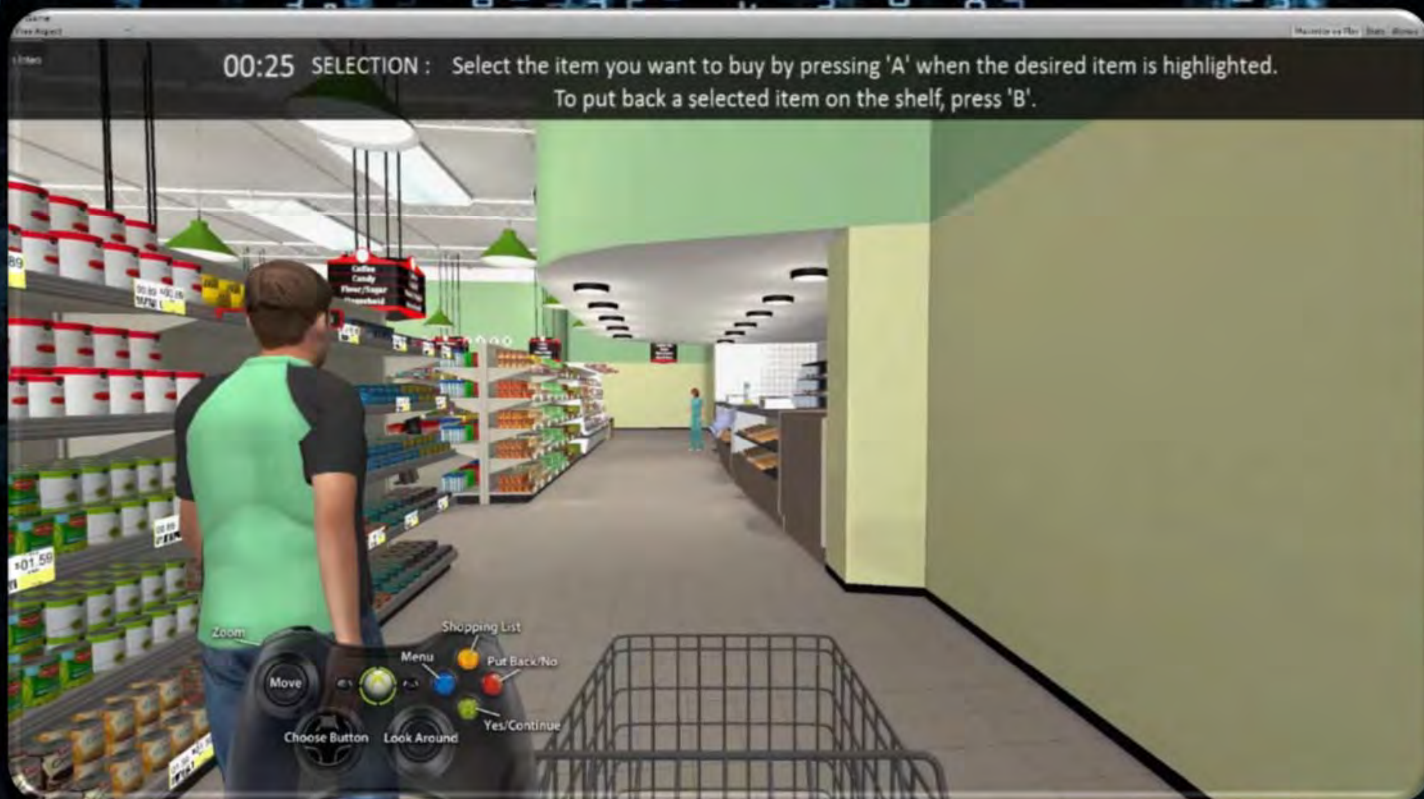
Department of Learning Disabilities, University of Nottingham
Queens Medical Centre, Clifton Boulevard
Nottingham, England NG7 2UH

INTRODUCTION:

**** Overview**

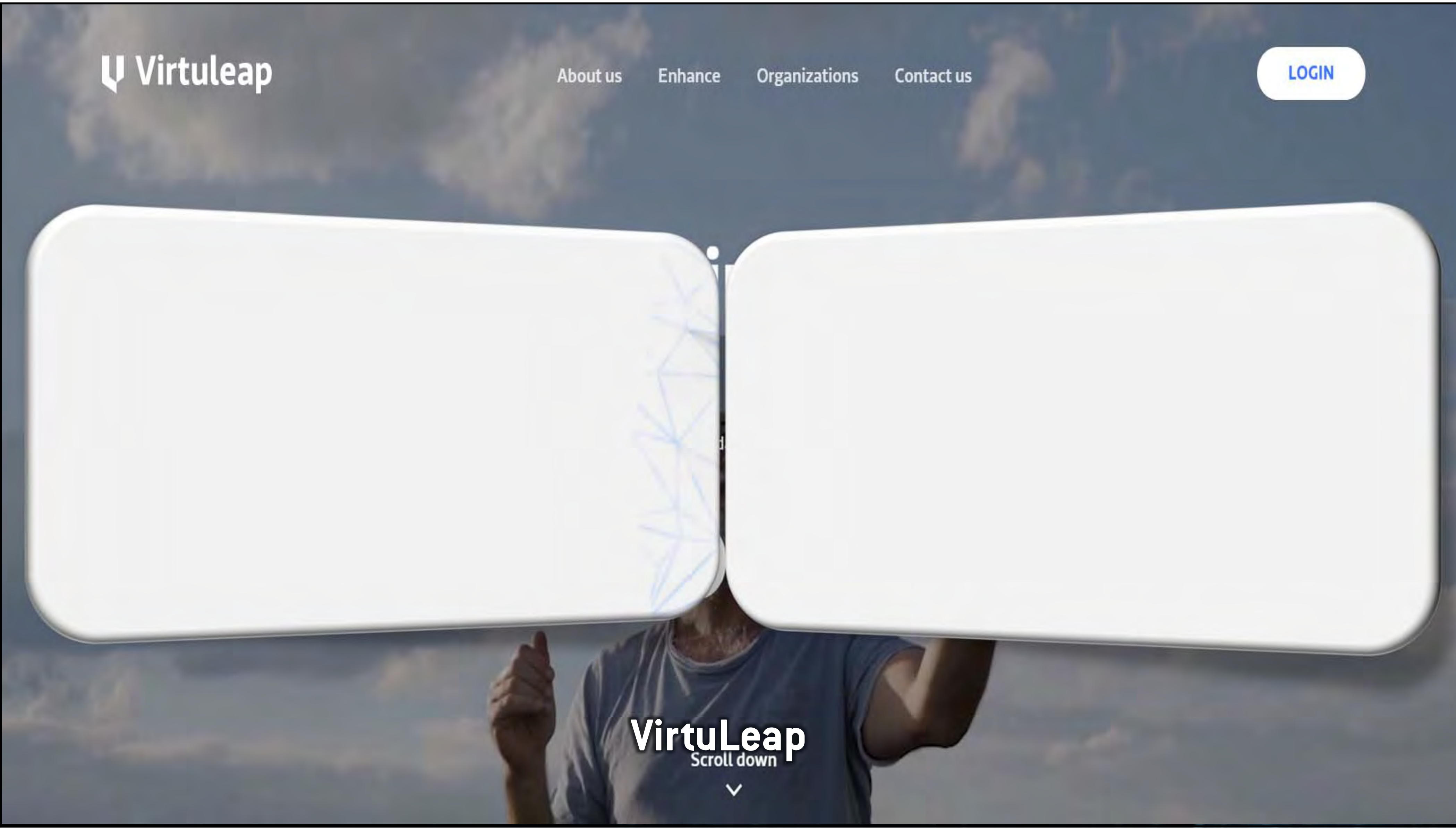
This paper describes a successful attempt to show generalisation to the real world of a skill practised in a desktop virtual environment. The people who took part in the study were a group of students with severe learning difficulties, who got better at a real supermarket shopping task after practising in a virtual supermarket.

The paper describes the special features of the people who took part, then draws upon developmental psychology to explain why virtual environments may be a particularly valuable tool in their education. The rationale for using desktop virtual environments in education is discussed, and the typical problems of producing generalisation and maintenance of learned skills amongst students with severe learning disabilities are outlined. Other attempts to show generalisation to the real world of skills acquired in virtual environments are reviewed, and the method and findings of our own work are presented and discussed.



Virtual Supermarket
Levy, Lok et al. 2016


Koenig et al. 2020
Katana Simulations


Virtuleap
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Organizations
Contact us
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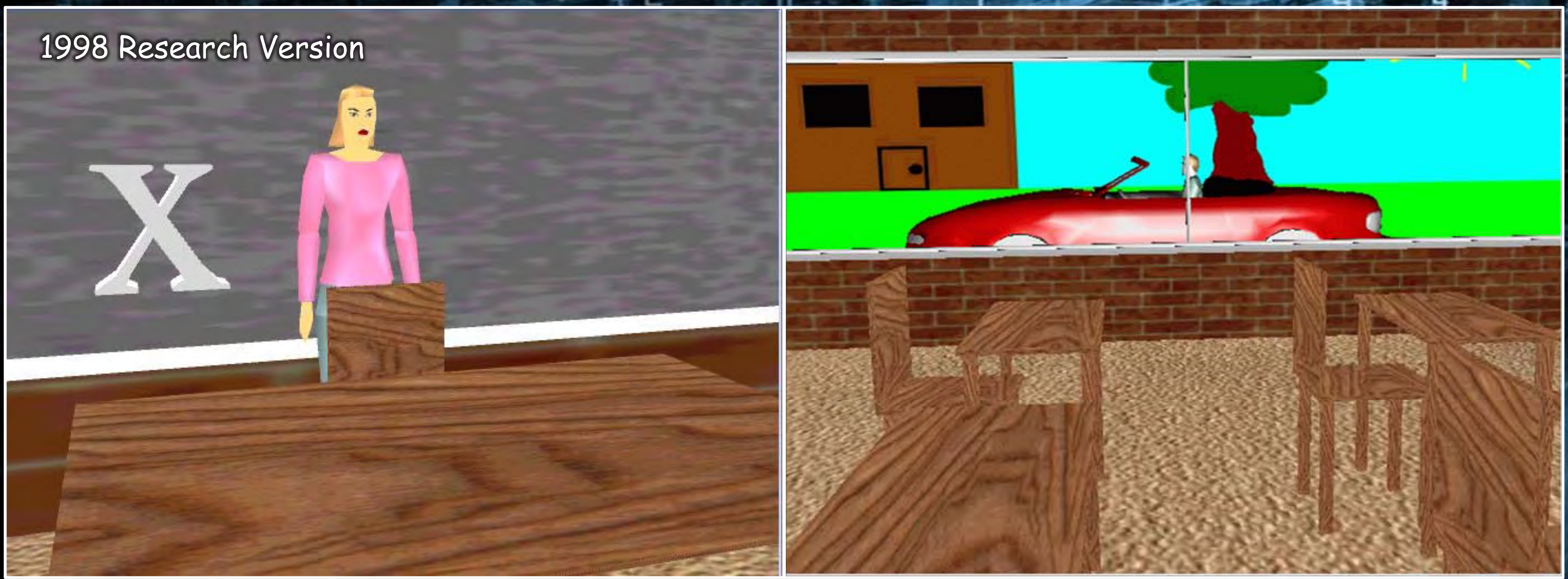
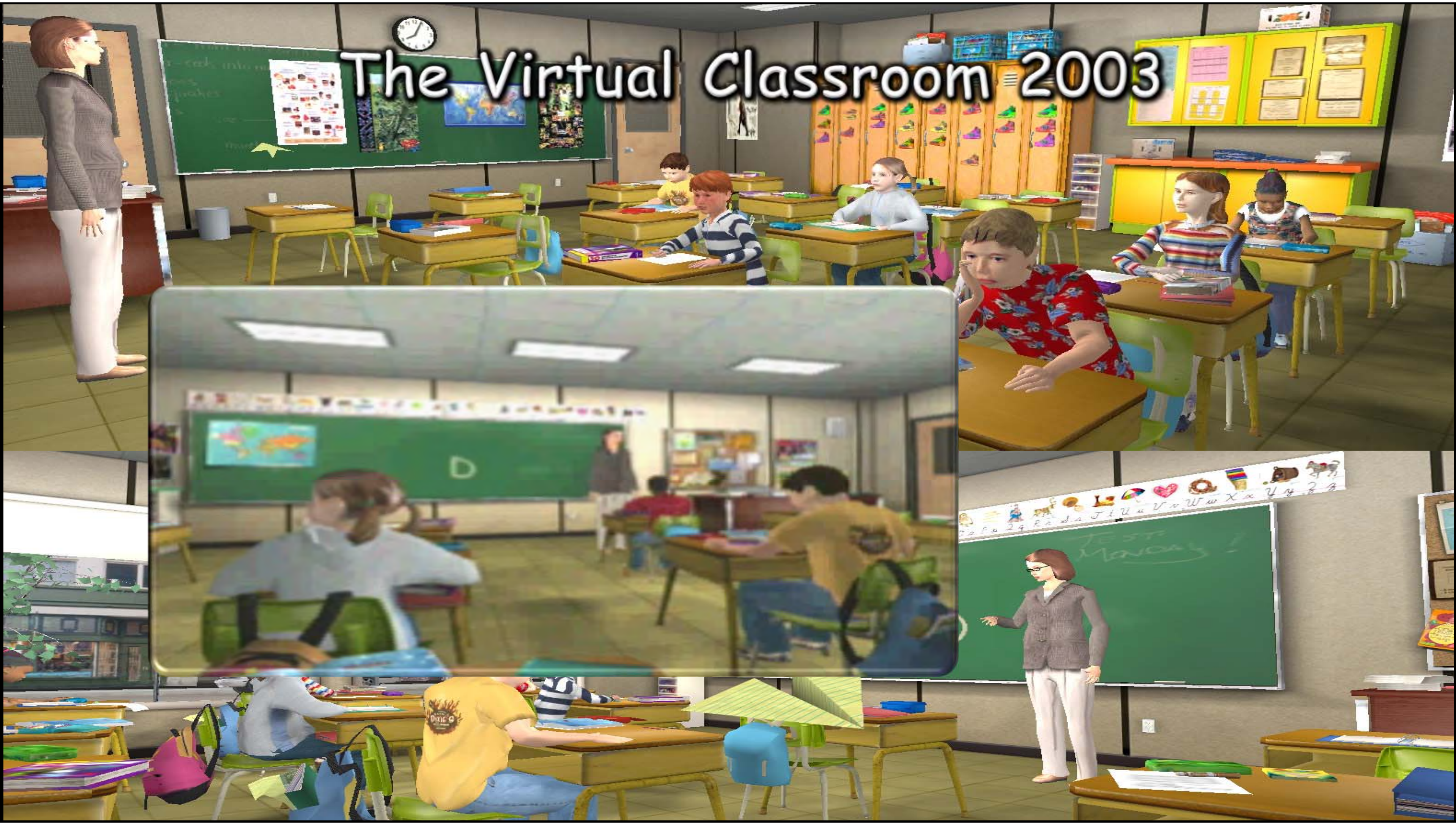
Scroll down

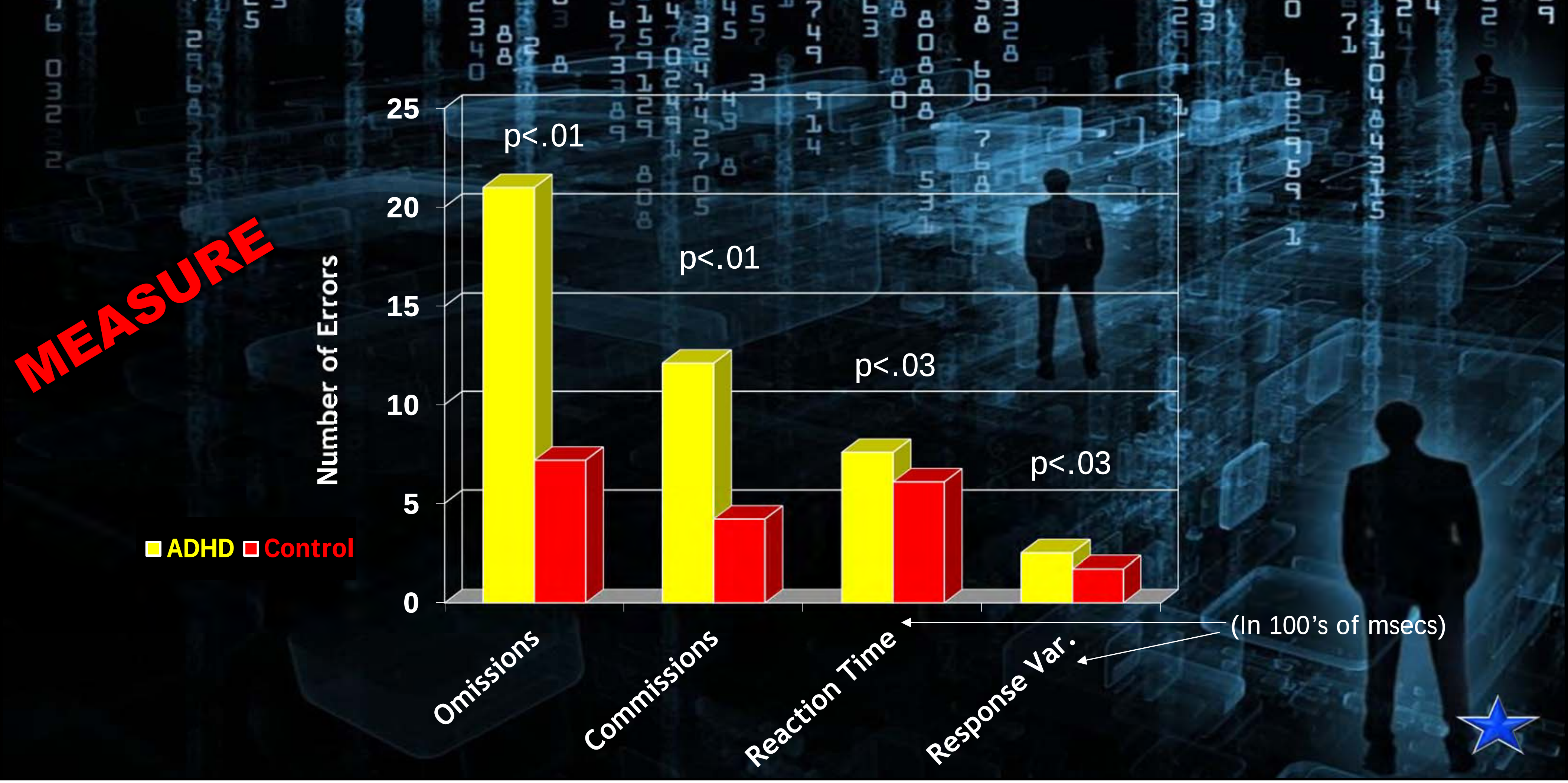

Virtual Classroom for Attention Process Assessment

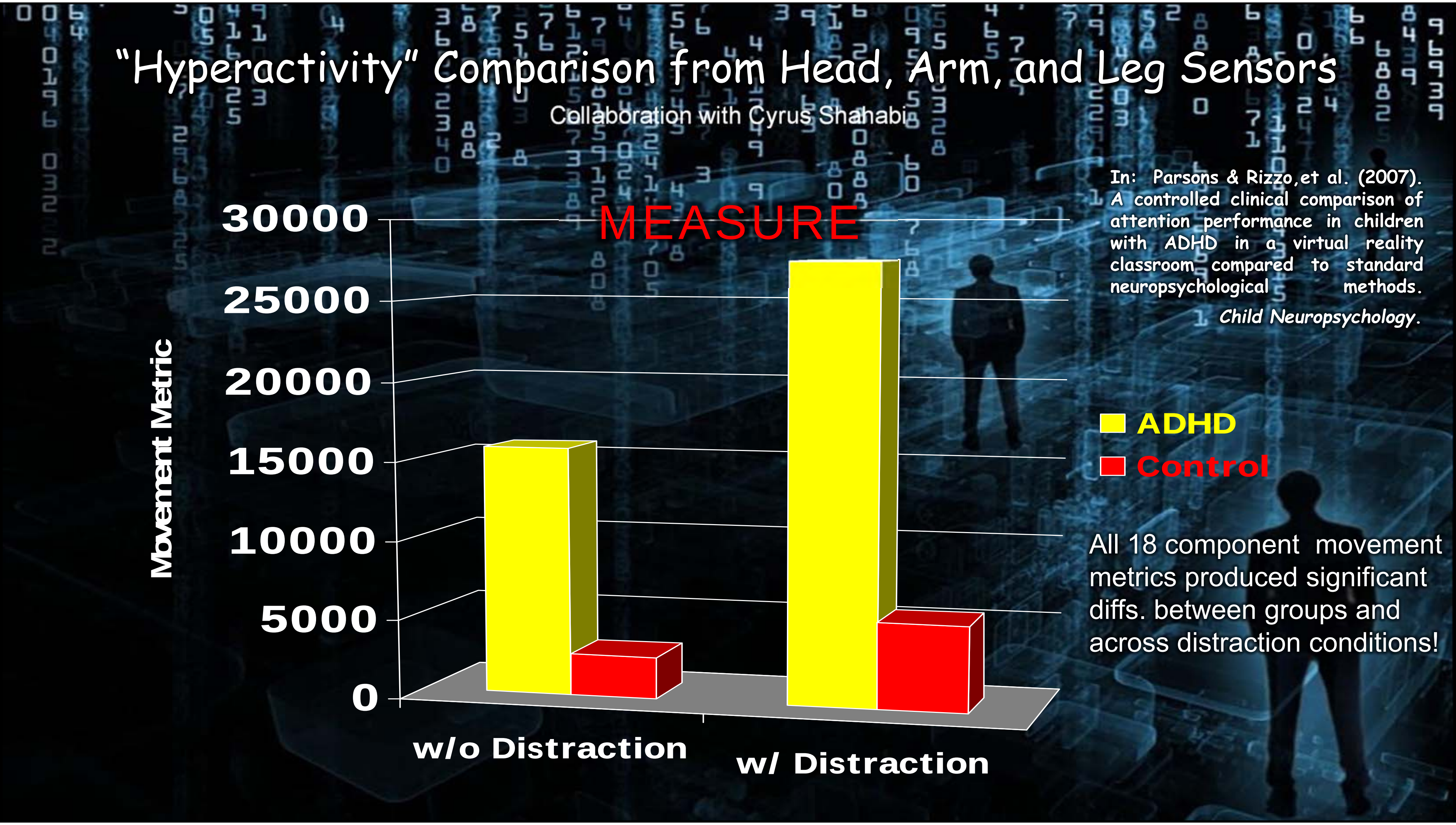
Origins of The Virtual Classroom 1998




The Virtual Classroom 2003

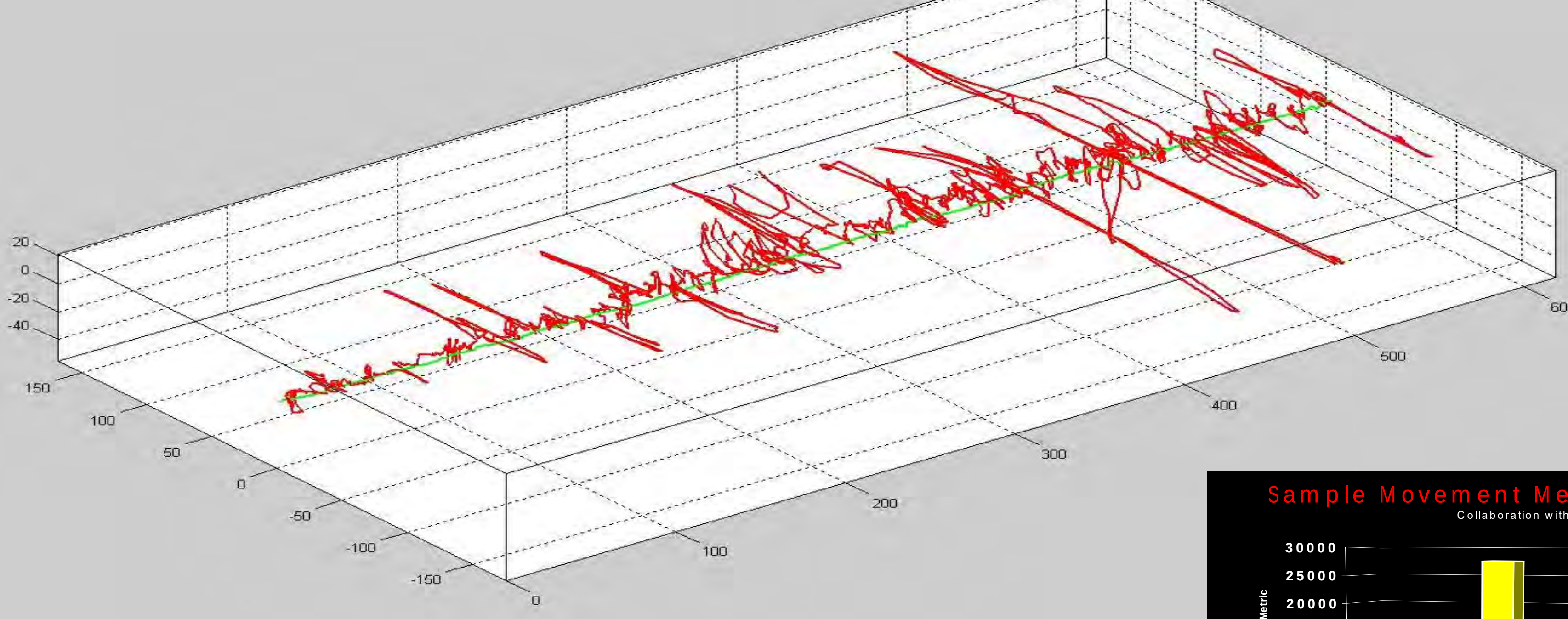
"AX" Attention Continuous Performance Task *with Distraction*

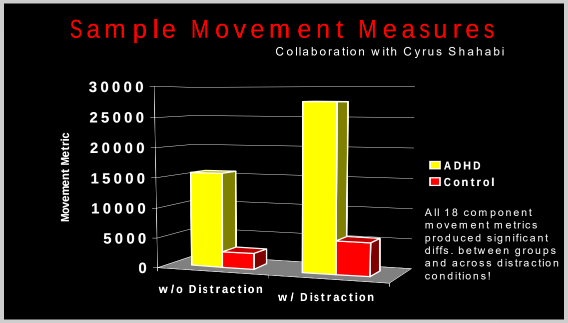



“Hyperactivity” Comparison from Head, Arm, and Leg Sensors
Collaboration with Cyrus Shahabi
MEASURE
In: Parsons & Rizzo, et al. (2007). A controlled clinical comparison of attention performance in children with ADHD in a virtual reality classroom compared to standard neuropsychological methods.
Child Neuropsychology.
Movement Metric
30000
25000
20000
15000
10000
5000
0
w/o Distraction
w/ Distraction
ADHD
Control
All 18 component movement metrics produced significant diffs. between groups and across distraction conditions!

VR Classroom Head Tracking Data

MEASURE





VR Classroom Head Tracking Demo

Neurotypical

ADHD

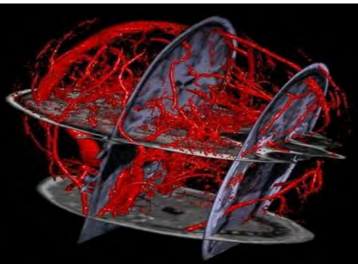
BTW, This is an actual 1992 U.S Postage Stamp!

Randomly selected ADHD and Control Subject Facing Blackboard during 10 min. vigilance trial.

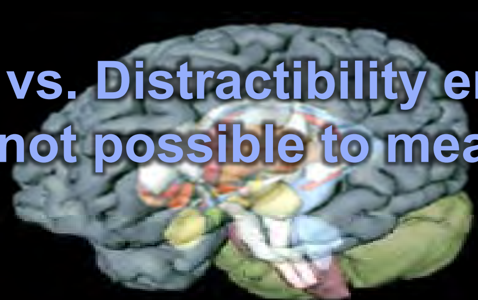
USC Institute for Creative Technologies

MedVRlab

Head Tracking Data



- Controls (n=10 X 20 Hit Stimuli per subject)
  - Missed 1 Out of 200 Hit Stimuli
  - .05% looking away from board during Hit Stimuli
- ADHD (n=8 X 20 Hit Stimuli per subject)
  - Missed 41 Out of 160 Hit Stimuli
  - 25% looking away from board during Hit Stimuli



Loss of FOCUS vs. Distractibility errors specified in a fashion that is not possible to measure without VR!

A Cognitive Leap...

into the Future!


COGNITIVE LEAP
New Version
H
C
T1
T2
Sneeze(3)
07:03

Current Steps/Future Visions

- Neurotypical Normative USA Sample (n=695; aged 6-13)
  - Successful Data Collection that reflects normal age-based developmental improvements.

Results from this normative sample showed clear linear performance improvements on all variables across the ages of 6-13, as was predicted across this developmental period. For example, when grouped by 2-year intervals, male participants showed a reduction of both omission and commission errors across the age groupings (for ages, 6-7, 8-9, 10-11, and 12-13, mean O's = 13.6, 6.6, 4.2, and 2.1, and mean C's = 22.5, 12.1, 5.4, and 2.9, respectively). Moreover, reaction time and reaction time variability produced similar reductions (mean RT's (in msecs.) = 523, 450, 407, and 402, and mean RTV's = 197, 149, 124, 110, respectively).

Normative Data for a Next Generation Virtual Classroom for Attention Assessment in Children with ADHD and Beyond!

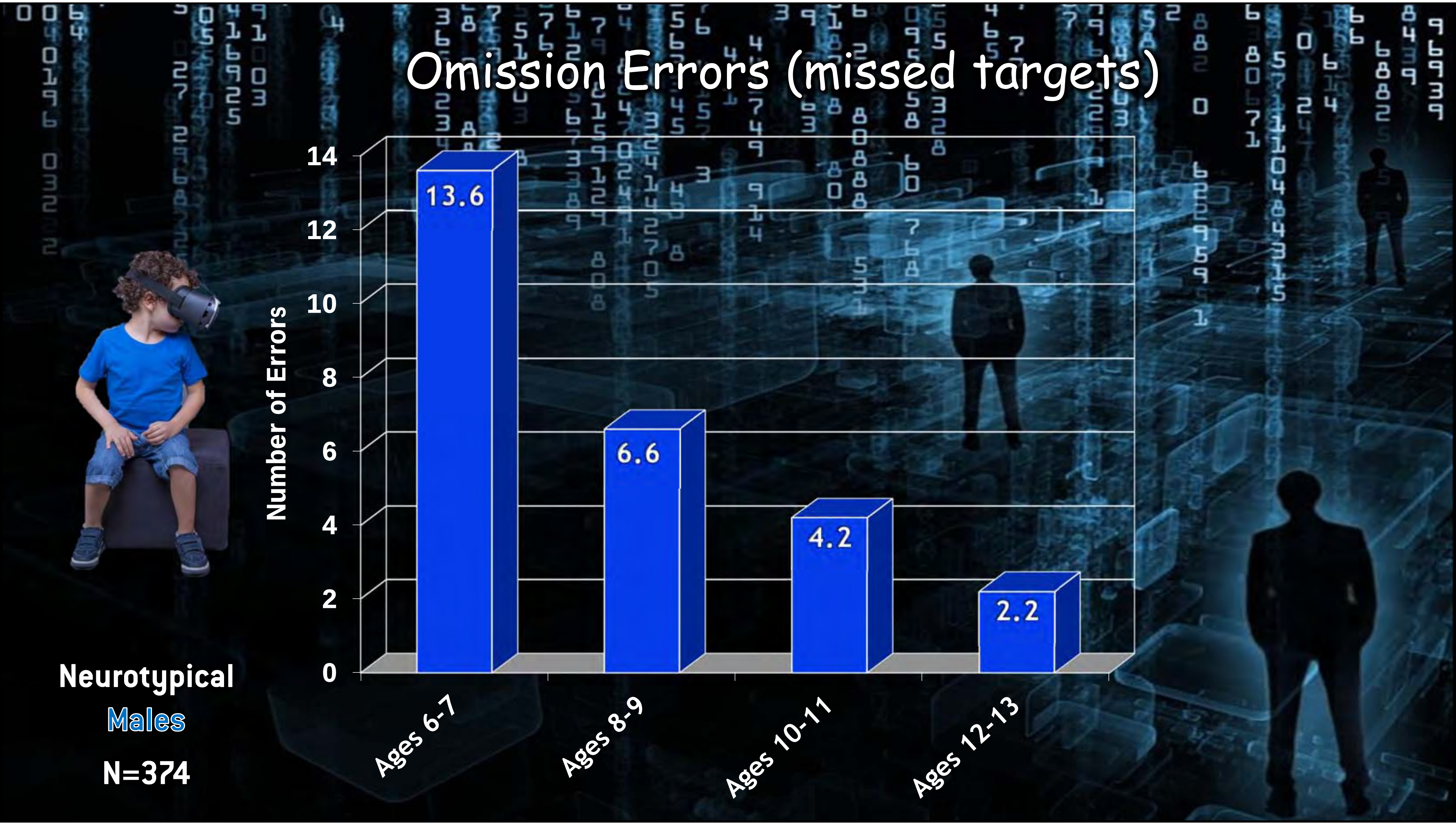
A Rizzo[1], J Z Chen[2], A Ma[2], J Wang[2], C-Y Chang[2], J Turnbull[3], C Shao[2]

[1]Institute for Creative Technologies, University of Southern California,
12015 East Waterfront Dr., Los Angeles, California, USA
[2]Cognitive Leap Solutions Inc.,
1110 S. Fifth Ave. Monrovia, California, USA
[3]Neurobehavior Services,
552 Crane Blvd., Los Angeles, California, USA

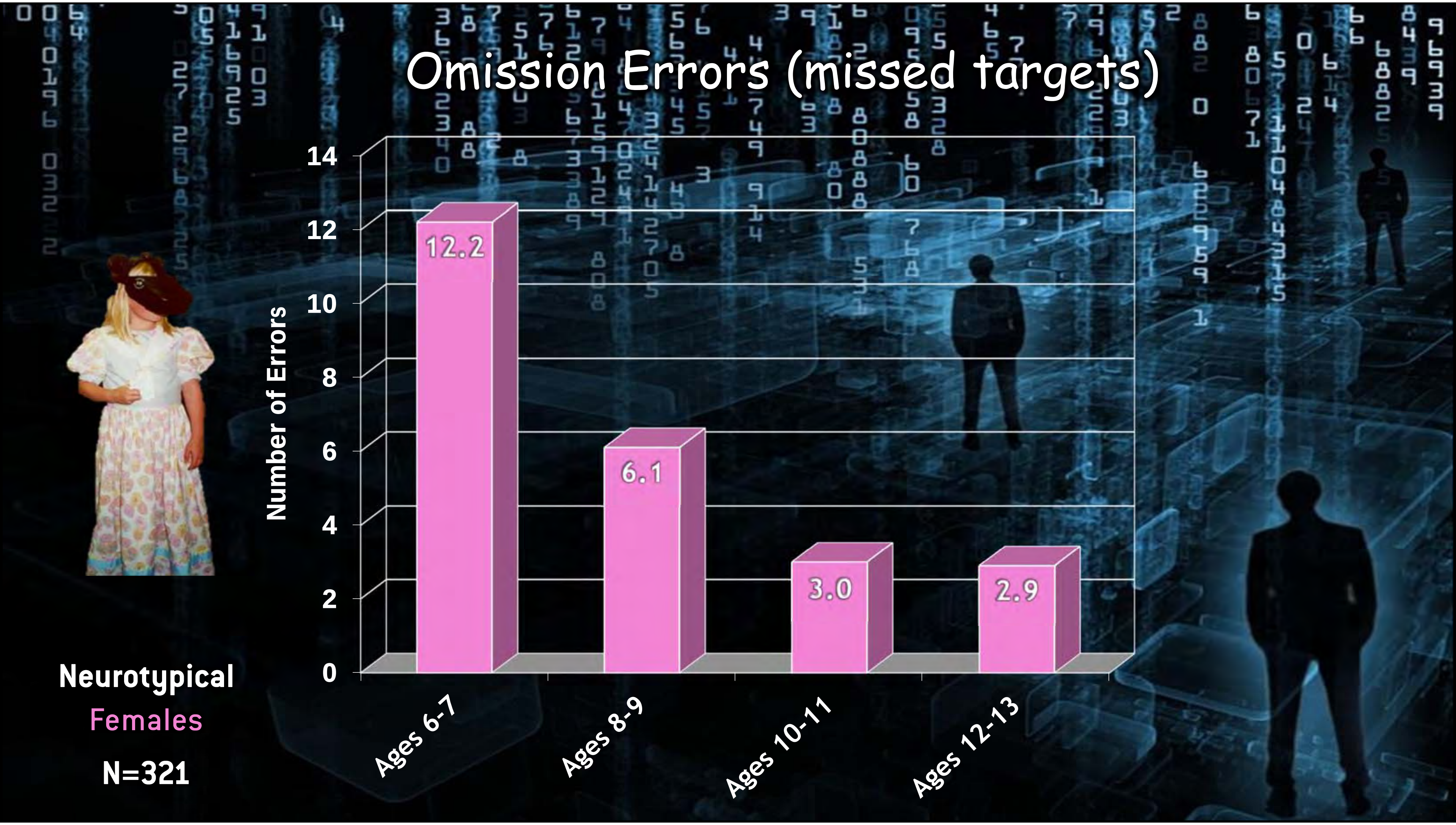
ABSTRACT

Numerous researchers and clinicians have recognized the unique match between Virtual Reality (VR) technology assets and the requirements of various clinical assessment and treatment approaches and an encouraging body of research has emerged. In the area of cognitive assessment related to central nervous system dysfunction, traditional approaches often rely on paper and pencil psychometric tests, qualitative ratings of behavior, and flat screen computer tests to inform diagnosis and to track changes in clinical status. VR offers options for enhancing the assessment process beyond these methods with the creation of standardized immersive simulations within which user performance can be consistently measured under conditions that may be more relevant to the challenges present in the real world, to better inform diagnostic and treatment decisions. Similar to traditional methods, normative data from typical children can be accumulated from VR simulations that provide performance standards for comparison with that of atypical children. This presentation will initially discuss the history of the USC Virtual Classroom (VC) (since 1998) for testing attention processes in children with ADHD and other neurological conditions. This will be followed by the presentation of a new version of the VC and the results from a neurotypical standardization sample of 695 children (age 6-13) tested in the VC. Ongoing data collection from children with attention impairments will be discussed in the context of the development of this research program.

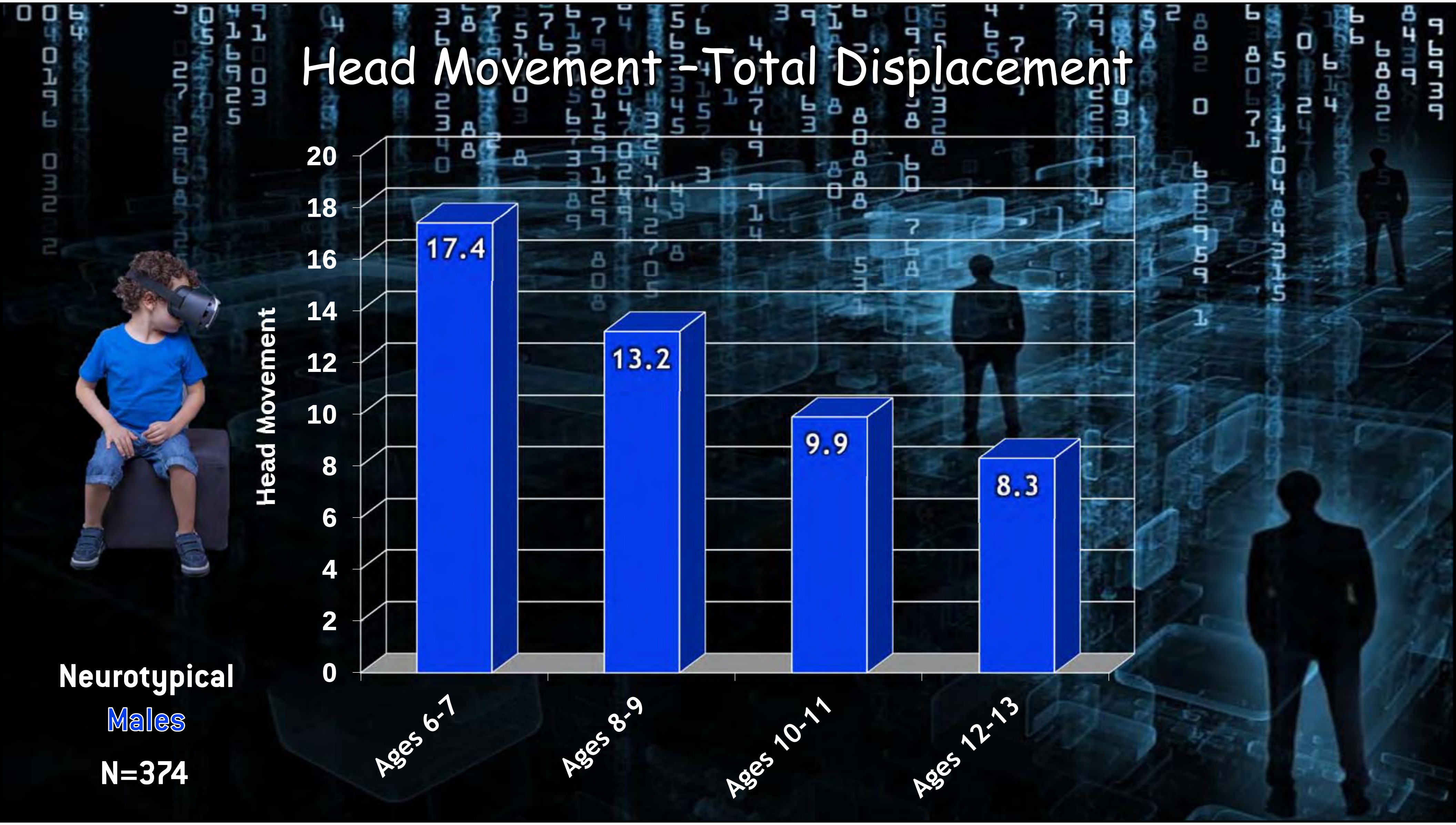
These findings provide support for the VC's capability to capture performance change over this span of early childhood development.



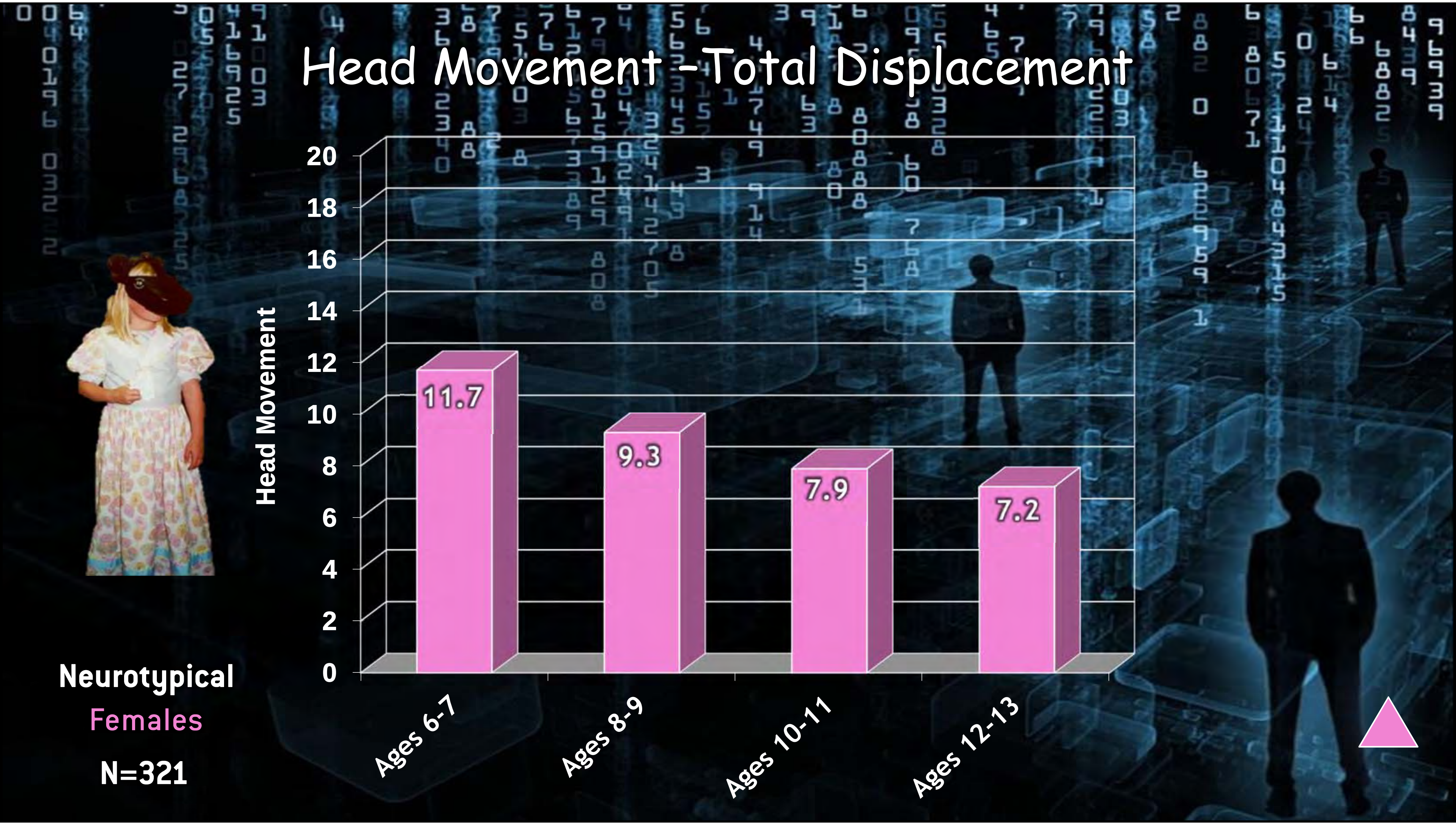
Omission Errors (missed targets)
Number of Errors
14
12
10
8
6
4
2
0
13.6
6.6
4.2
2.2
Ages 6-7
Ages 8-9
Ages 10-11
Ages 12-13
Neurotypical
Males
N=374



Omission Errors (missed targets)
Number of Errors
14
12
10
8
6
4
2
0
12.2
6.1
3.0
2.9
Ages 6-7
Ages 8-9
Ages 10-11
Ages 12-13
Neurotypical
Females
N=321



Head Movement –Total Displacement
Head Movement
20
18
16
14
12
10
8
6
4
2
0
17.4
13.2
9.9
8.3
Ages 6-7
Ages 8-9
Ages 10-11
Ages 12-13
Neurotypical
Males
N=374



Head Movement –Total Displacement
Head Movement
20
18
16
14
12
10
8
6
4
2
0
11.7
9.3
7.9
7.2
Ages 6-7
Ages 8-9
Ages 10-11
Ages 12-13
Neurotypical
Females
N=321

Virtual Classroom Publications

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- Bioulac, S., Micoulaud-Franchi, J-A., Maire, J., Bouvard, M.P., **Rizzo, A.A,,** Sagaspe, P., and Philip, P. (2018). Virtual remediation versus methylphenidate to improve distractibility in children with ADHD: A controlled randomized clinical trial study. *Journal of Attention Disorders*.
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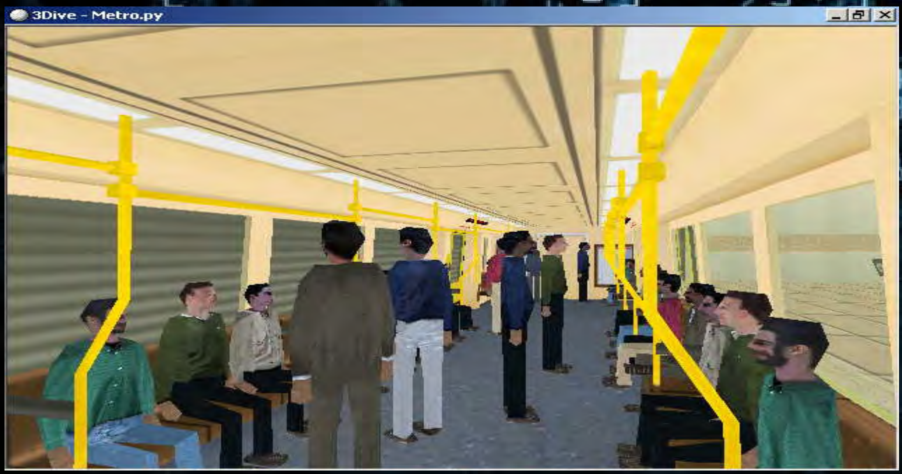
7. Benefit from Virtual Human interaction!

Panic disorder and agoraphobia



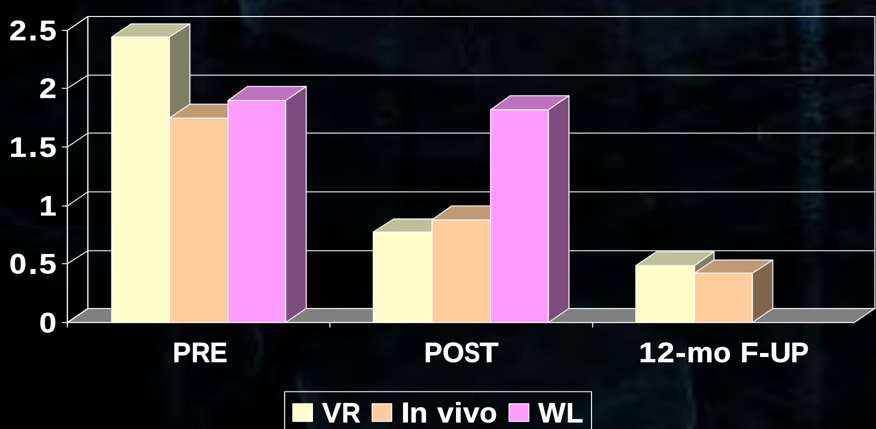
Botella et al., 1999

Panic disorder and agoraphobia

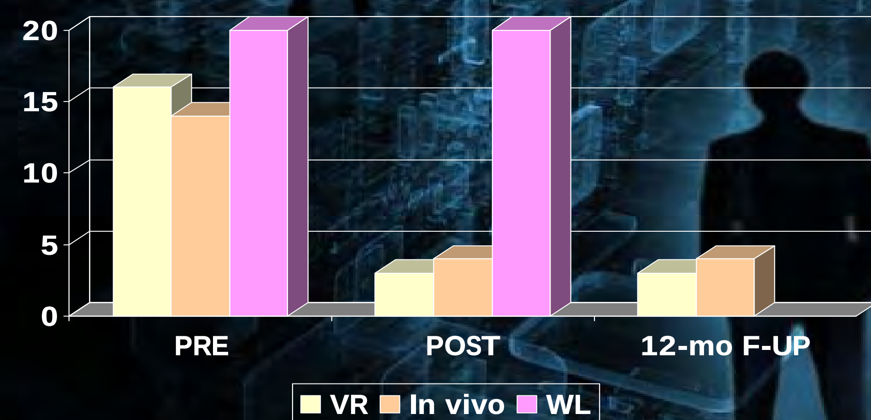
N = 36. All p < .001.   90 and 91% panic-free at follow-up.

Botella et al. (2007)

PDSS



FQ-Ago



Virtual Human Exposure as good as the real thing!

Social phobia

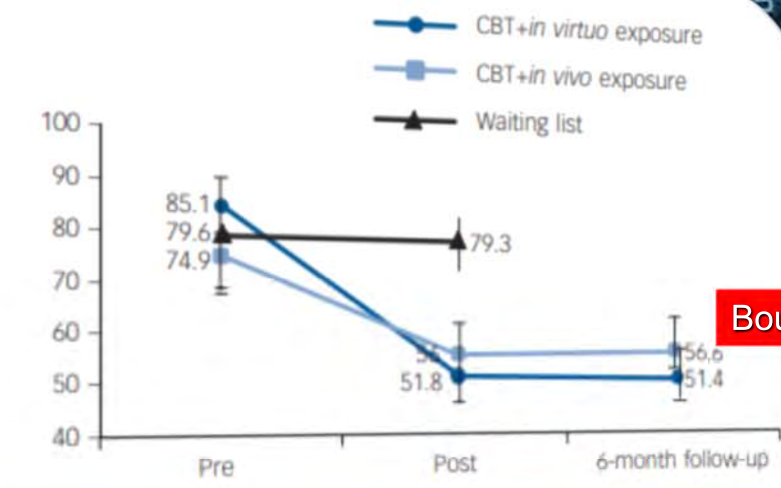


Fig. 2 The results on the main outcome measure (Liebowitz Social Anxiety Scale-SR) comparing cognitive–behavioural therapy (CBT) with exposure delivered in virtual reality (*in virtuo*), without virtual reality (*in vivo*) and a waiting list.

Bouchard et al. (2017)

BJPsych The British Journal of Psychiatry (2017) 210, 276–283. doi: 10.1192/bjp.bp.116.184234

Virtual reality compared with *in vivo* exposure in the treatment of social anxiety disorder: a three-arm randomised controlled trial[†]

Stéphane Bouchard, Stéphanie Dumoulin, Geneviève Robillard, Tanya Guitard, Évelyne Klinger, Hélène Forget, Claudie Loranger and François Xavier Roucaut

Background
People with social anxiety disorder (SAD) fear social … may be reluctant to seek treatments … to social situations. Social exposure … al reality (VR), embedded in individual … al therapy (CBT), could be an answer.

Aims
To show that conducting VR exposure in CBT for SAD is effective and is more practical for therapists than conducting exposure *in vivo*.

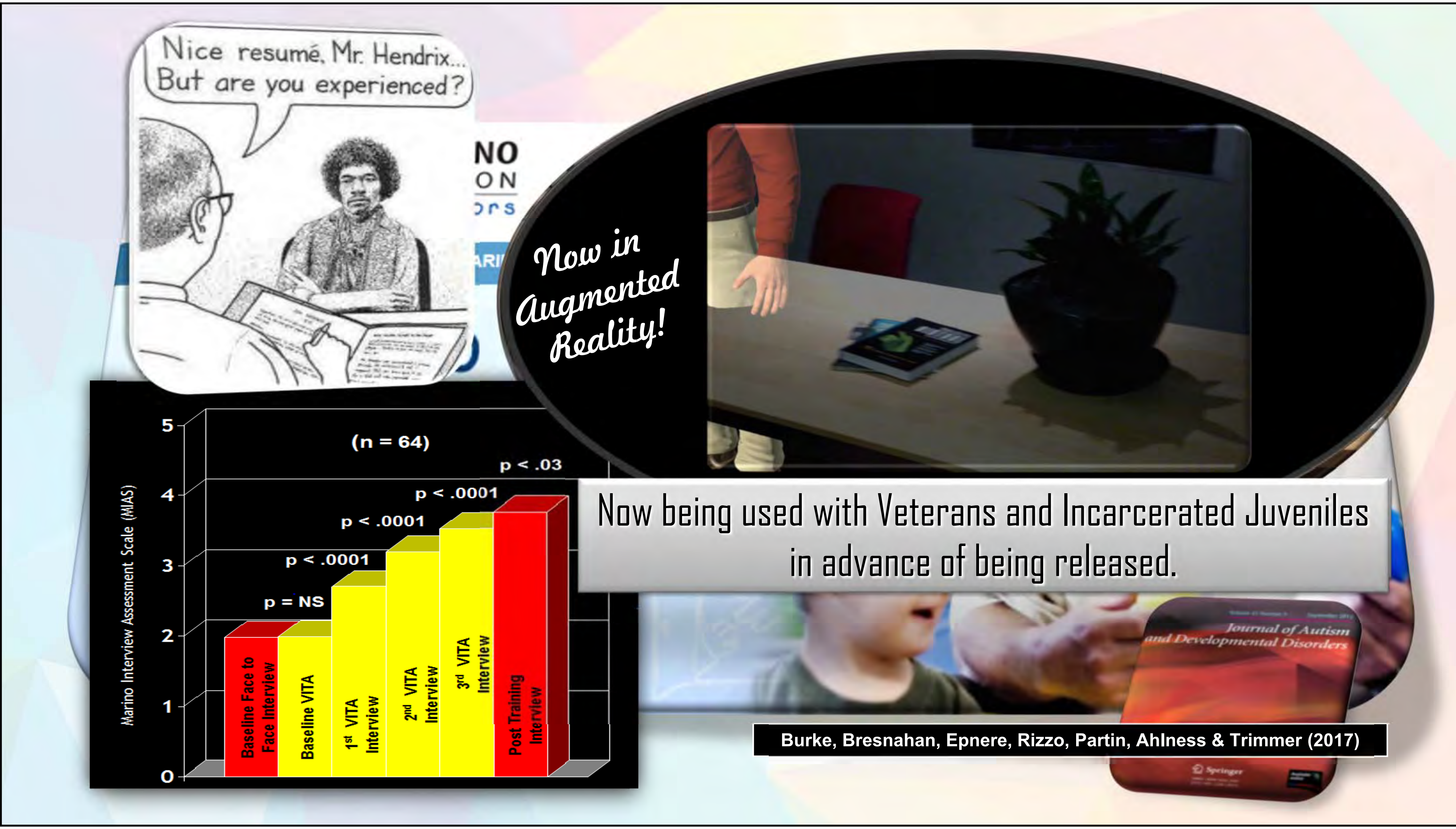
Method
Participants were randomly assigned to either VR exposure (*n* = 17), *in vivo* exposure (*n* = 22) or waiting list (*n* = 20). Participants in the active arms received individual CBT for 14 weekly sessions and outcome was assessed with questionnaires and a behaviour avoidance test. (Trial registration number ISRCTN99747069.)

Results
Improvements were found on the primary (Liebowitz Social Anxiety Scale) and all five secondary outcome measures in both CBT groups compared with the waiting list. Conducting exposure in VR was more effective at post-treatment than *in vivo* on the primary outcome measure and on one secondary measure. Improvements were maintained at the 6-month follow-up. VR was significantly more practical for therapists than *in vivo* exposure.

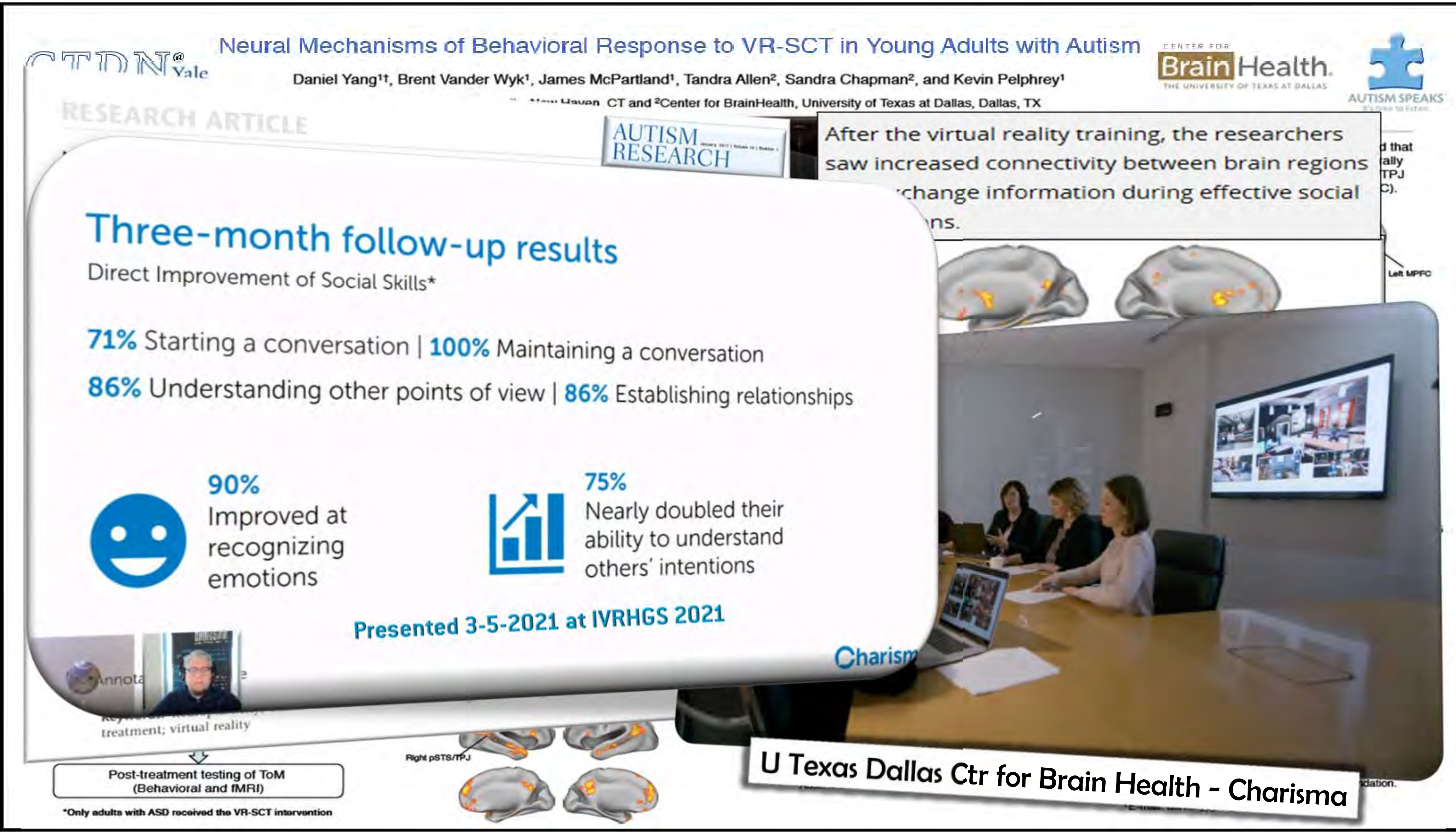
Conclusions
Using VR can be advantageous over standard CBT as a potential solution for treatment avoidance and as an efficient, cost-effective and practical medium of exposure.

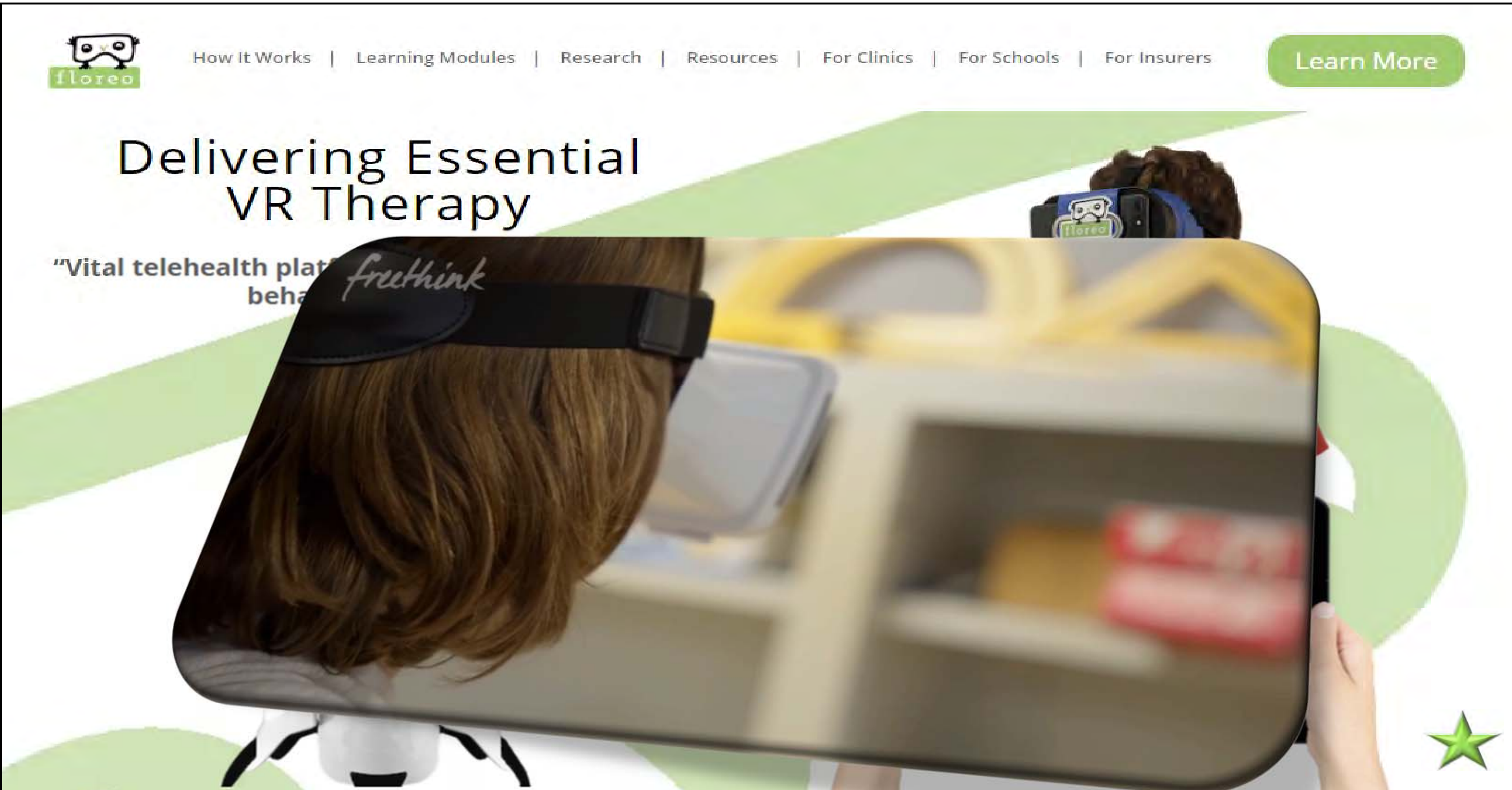
Declaration of interest
S.B. and G.R. are consultants to and own equity in Cliniques et Développement in Virtuo, which develops virtual environments; however, Cliniques et Développement in Virtuo did not create the virtual environments used in this study. The terms of these arrangements were reviewed and approved by Université du Québec en Outaouais, in accordance with its policy on conflicts of interest.

“Conducting exposure in VR was MORE effective at post treatment than in vivo on the primary outcome measure”



Nice resumé, Mr. Hendrix...
But are you experienced?
Now in Augmented Reality!
Marino Interview Assessment Scale (MIAS)
(n = 64)
p = NS
p < .0001
p < .0001
p < .0001
p < .03
Baseline Face to Face Interview
Baseline VITA
1st VITA Interview
2nd VITA Interview
3rd VITA Interview
Post Training Interview
0
1
2
3
4
5
Now being used with Veterans and Incarcerated Juveniles in advance of being released.
Journal of Autism and Developmental Disorders
Burke, Bresnahan, Epnere, Rizzo, Partin, Ahlness & Trimmer (2017)


Neural Mechanisms of Behavioral Response to VR-SCT in Young Adults with Autism
Daniel Yang[1†], Brent Vander Wyk[1], James McPartland[1], Tandra Allen[2], Sandra Chapman[2], and Kevin Pelphrey[1]
CT and [2]Center for BrainHealth, University of Texas at Dallas, Dallas, TX
Yale
Center for BrainHealth
THE UNIVERSITY OF TEXAS AT DALLAS
AUTISM SPEAKS
RESEARCH ARTICLE
AUTISM RESEARCH
After the virtual reality training, the researchers saw increased connectivity between brain regions
change information during effective social
Three-month follow-up results
Direct Improvement of Social Skills*
71% Starting a conversation | 100% Maintaining a conversation
86% Understanding other points of view | 86% Establishing relationships
90% Improved at recognizing emotions
75% Nearly doubled their ability to understand others' intentions
Presented 3-5-2021 at IVRHGS 2021
Charism
treatment; virtual reality
Post-treatment testing of ToM (Behavioral and fMRI)
*Only adults with ASD received the VR-SCT intervention
Right pSTS/TPJ
Left MPFC
U Texas Dallas Ctr for Brain Health - Charisma



Direct Training for Dealing with the Stress of a Police Encounter

IN THE WINGS JANUARY 8, 2018 ISSUE

STANDARDIZED PATIENTS AND THE ART OF MEDICAL MALADIES

Actors train hard to portray specific illnesses and psychiatric disorders, sometimes even with heroin tracks of makeup.

By David Owen January 1, 2018

THE NEW YORKER

Health & Science

Demand is high for pretend patients

The Washington Post
Democracy Dies in Darkness

By Lena H. Sun
October 13, 2011

Ted Bell knew his portrayal of a depressed, elderly patient was convincing when the medical student who was examining him broke down in tears. Her instructors had to call a timeout because his flat monotone and unkempt appearance reminded her too much of her father, who had similar symptoms.

Virtual Patients Lab

Virtual Patients – Military and Civilian Applications

SickCall

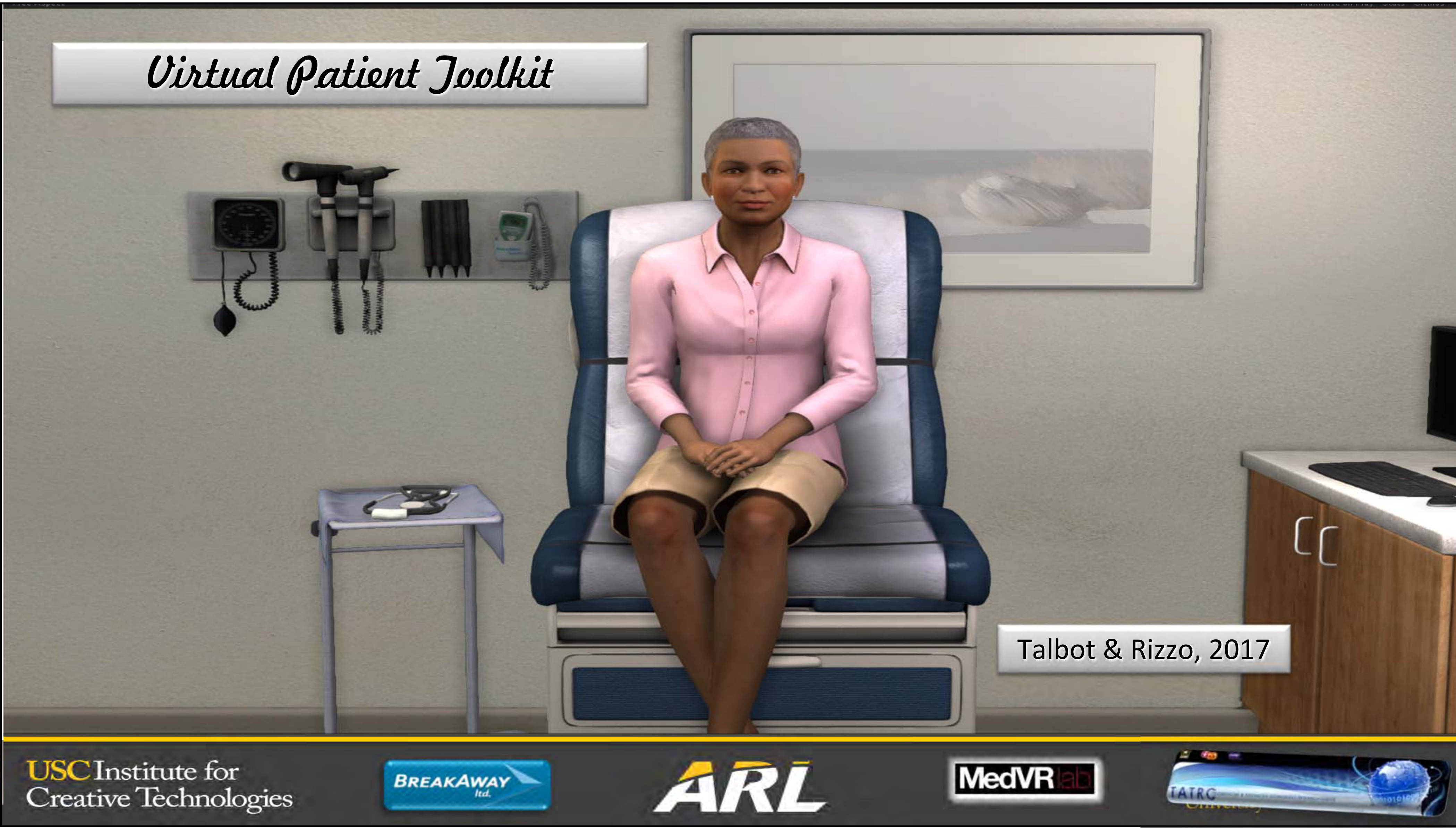
Collaboration with the USC School of Social Work Masters in Military Social Work Program

Justin

Justina

Virtual Patients w/USC Psychiatry

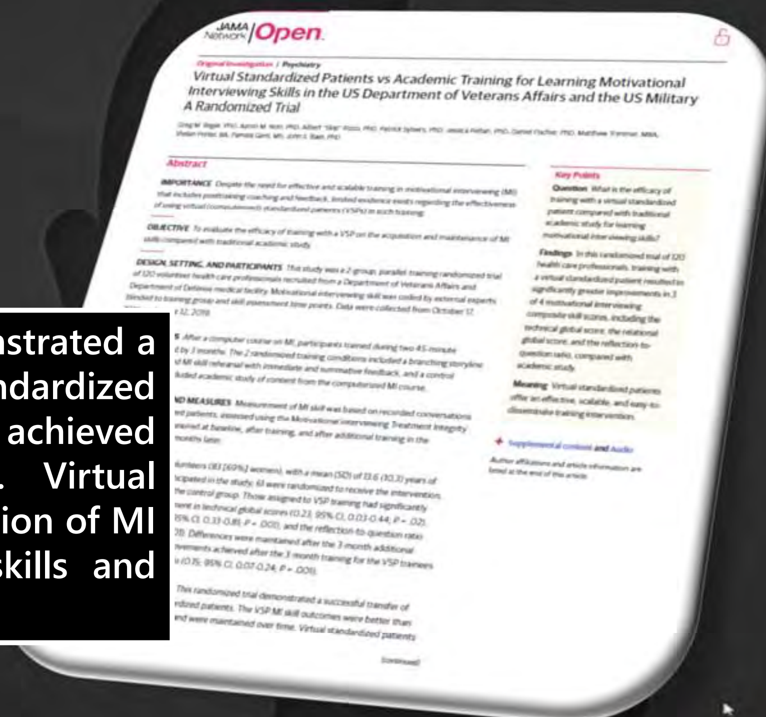
MedVRlab


Virtual Patient Toolkit
Talbot & Rizzo, 2017
USC Institute for Creative Technologies
BREAKAWAY ltd.
ARL
MedVR lab

Teach
Virtual Patient Toolkit
USC Institute for Creative Technologies
BreakAway ltd.
ARL
MedVR lab
TATRC

Virtual Patients Lab

MIND: Motivational Interviewing Novice Demonstration Simulation


JAMA Network | Open

Virtual Standardized Patients vs Academic Training for Learning Motivational Interviewing Skills in the US Department of Veterans Affairs and the US Military

A Randomized Trial

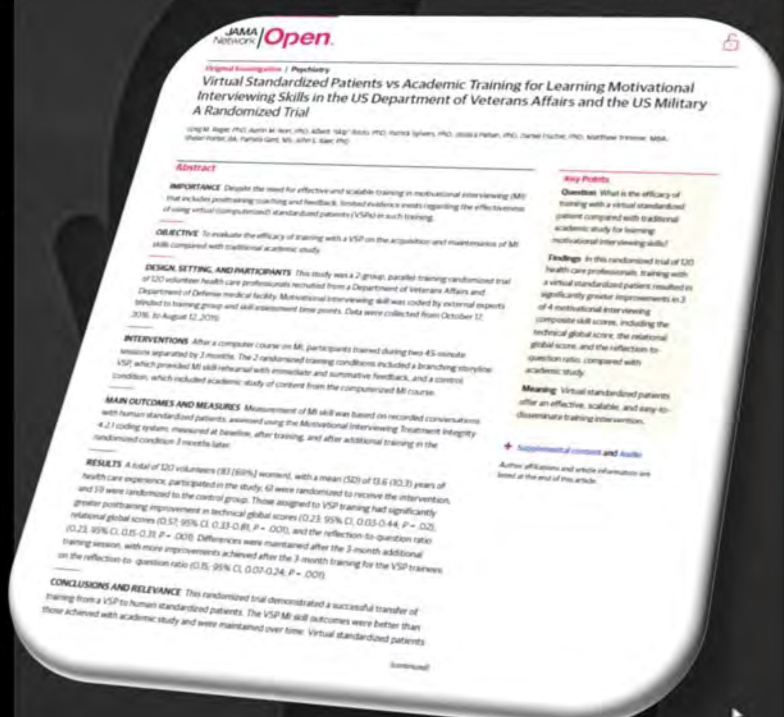
"CONCLUSIONS AND RELEVANCE: This randomized trial demonstrated a successful transfer of training from a VSP to human standardized patients. The VSP MI skill outcomes were better than those achieved with academic study and were maintained over time. Virtual standardized patients have the potential to facilitate dissemination of MI and may be useful for training in other evidence-based skills and treatments."

Reger, Norr, Rizzo, Sylvers, Peltan, Fischer, Trimmer, Porter, Gant, & Baer, 2020

Virtual Patients Lab

MIND: Motivational Interviewing Novice Demonstration Simulation

- **Randomized Controlled Trial (RCT) between: VA online training + 45 minutes review vs. VA online training + MIND VH Training**
- **N=126**
- **Live Actor patient assessment at BASELINE, Post Training 1, Post 3 Month Follow Up**
- **“Blinded” Expert Ratings of Live Performance**
- **Self report ratings on Confidence, Satisfaction with Training, and Self-efficacy**
- **VH group outperformed on 3 core metrics of performance pre to post and pre to 3 month FU**
- **Significantly higher satisfaction with VH training**
- **Equivalent ratings of confidence and self-efficacy**
- **NIH-Funded VA Suicide Prevention Training**


JAMA Network Open

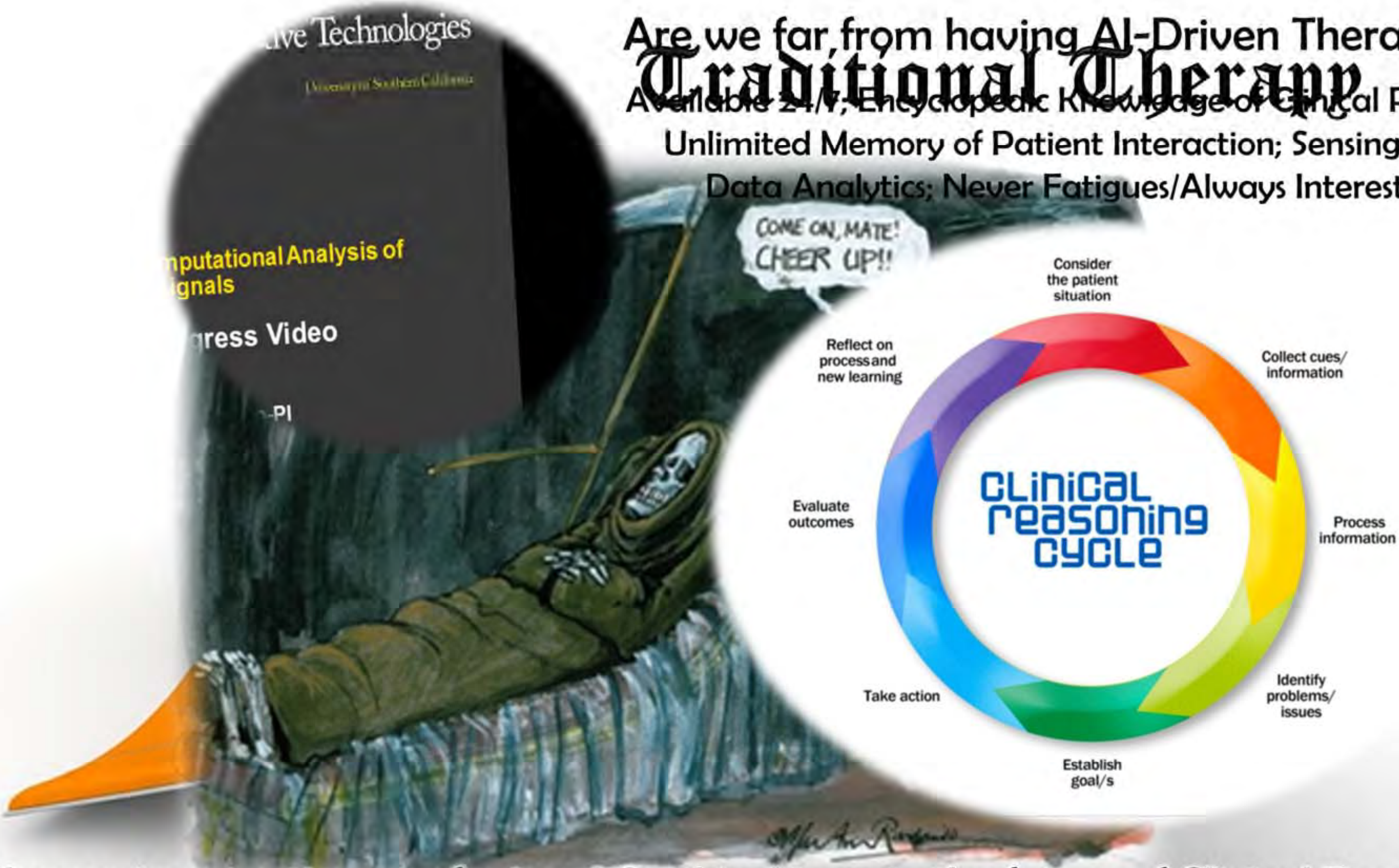
Virtual Standardized Patients vs Academic Training for Learning Motivational Interviewing Skills in the US Department of Veterans Affairs and the US Military
A Randomized Trial

Reger, Norr, Rizzo, Sylvers, Peltan, Fischer, Trimmer, Porter, Gant, & Baer, 2020

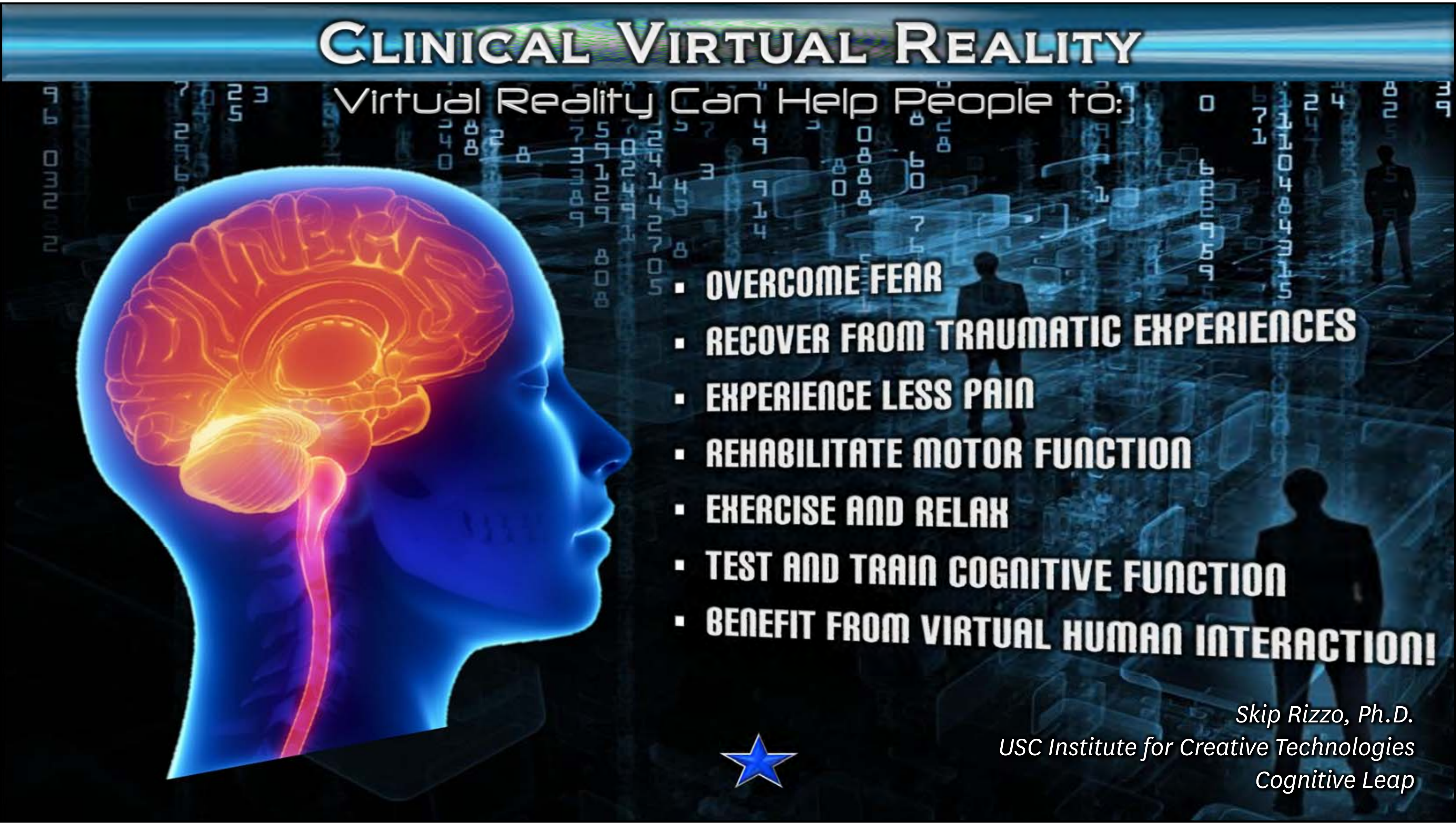
Are we far from having AI-Driven Therapists?

Traditional Therapy

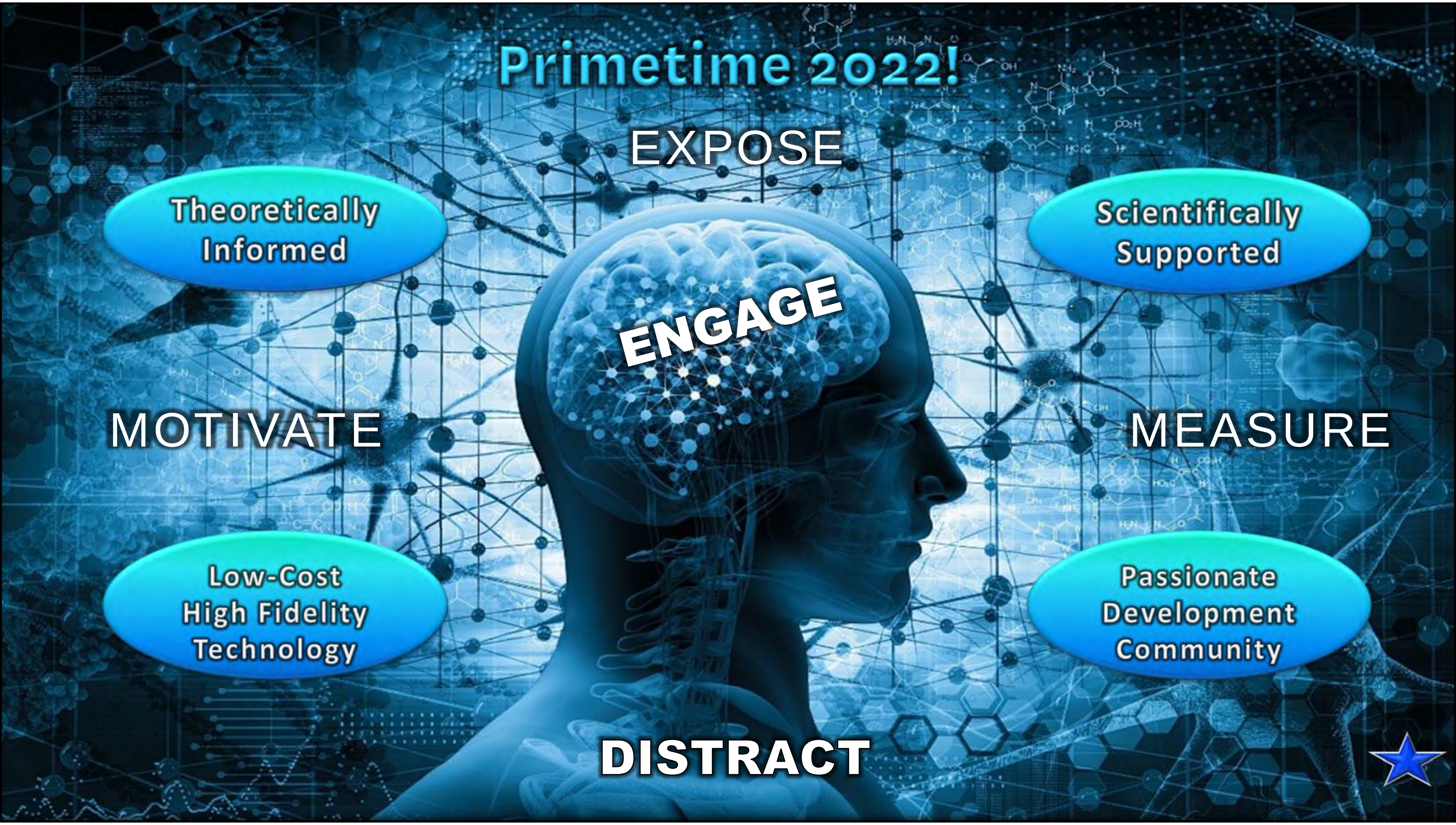
Available 24/7; Encyclopedic Knowledge of Clinical Processes; Unlimited Memory of Patient Interaction; Sensing & Big Data Analytics; Never Fatigues/Always Interested!



Likely the most contentious professional & ethical issue in the future of Clinical Psychology!


CLINICAL VIRTUAL REALITY
Virtual Reality Can Help People to:
▪ OVERCOME FEAR
▪ RECOVER FROM TRAUMATIC EXPERIENCES
▪ EXPERIENCE LESS PAIN
▪ REHABILITATE MOTOR FUNCTION
▪ EXERCISE AND RELAX
▪ TEST AND TRAIN COGNITIVE FUNCTION
▪ BENEFIT FROM VIRTUAL HUMAN INTERACTION!
Skip Rizzo, Ph.D.
USC Institute for Creative Technologies
Cognitive Leap


CLINICAL VIRTUAL REALITY
EXPOSE
ENGAGE
MOTIVATE
MEASURE
DISTRACT

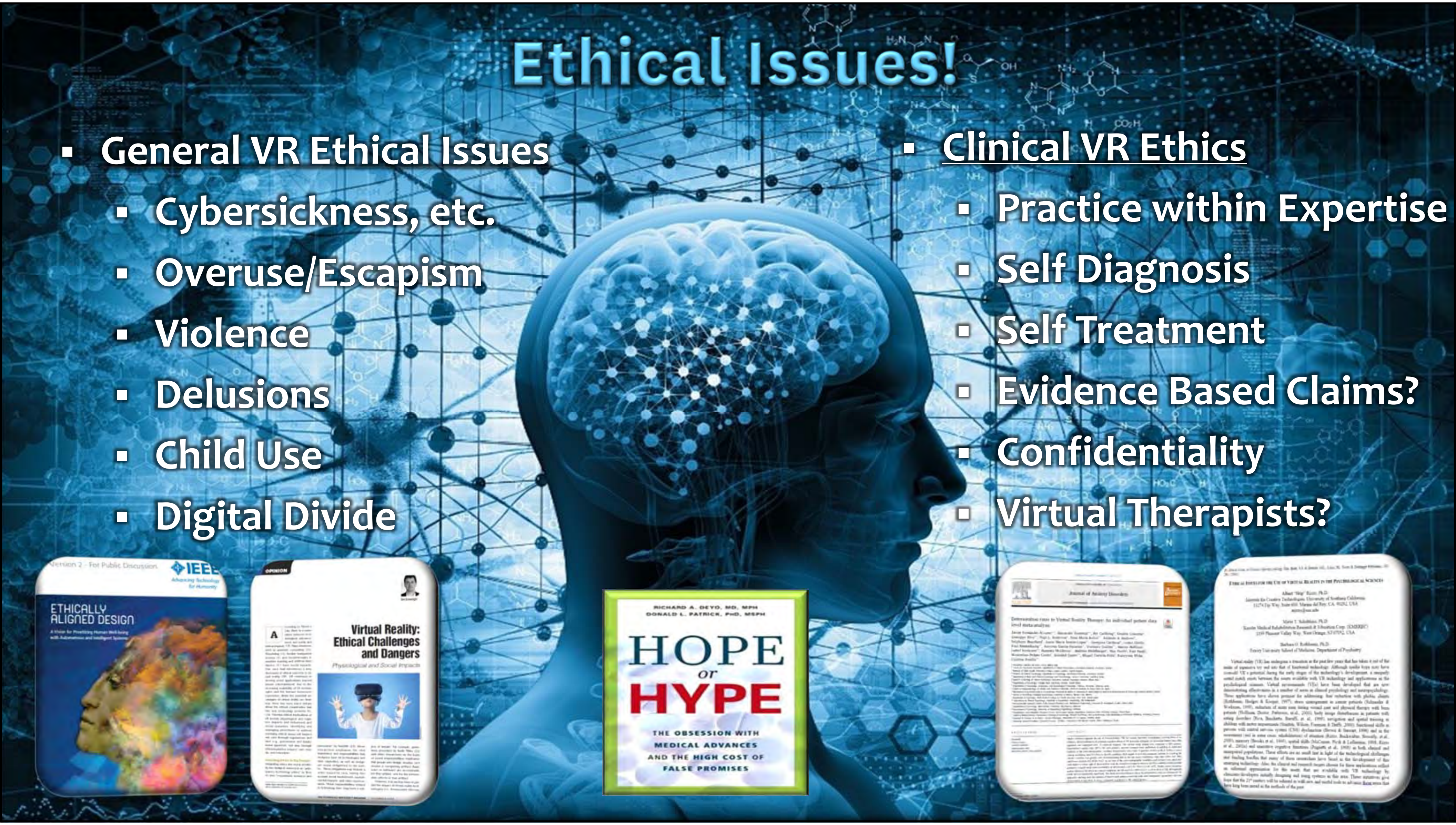

Primetime 2022!
EXPOSE
Theoretically Informed
Scientifically Supported
ENGAGE
MOTIVATE
MEASURE
Low-Cost High Fidelity Technology
Passionate Development Community
DISTRACT

Clinician's Weigh-in!

According to a poll of 70 psychotherapy experts...

"*When clinicians were surveyed as to interventions predicted to increase in the next decade, VR ranked 4th out of 45 options with other computer-supported methods occupying 4 out of the top 5 positions.*"

2013 **Norcross JC, Pfund RA, Prochaska JO. (2013). Psychotherapy in 2022. A Delphi poll on its future. Professional Psychology: Research & Practice. 44(5):363-70.**



Ethical Issues!
General VR Ethical Issues
Cybersickness, etc.
Overuse/Escapism
Violence
Delusions
Child Use
Digital Divide
Clinical VR Ethics
Practice within Expertise
Self Diagnosis
Self Treatment
Evidence Based Claims?
Confidentiality
Virtual Therapists?
Version 2 - For Public Discussion
IEEE
ETHICALLY ALIGNED DESIGN
OPINION
Virtual Reality: Ethical Challenges and Dangers
Physiological and Social Impacts
RICHARD A. DEYO, MD, MPH
DONALD L. PATRICK, PhD, MSPH
HOPE or HYPE
THE OBSESSION WITH MEDICAL ADVANCES AND THE HIGH COST OF FALSE PROMISES
Journal of Anxiety Disorders


Metaverse Hype or Help!??
Polygon
1997
Active Worlds
“One day son, all this will be yours.”
PERCIVAL
Metaverse and virtual reality are gaining a foothold in healthcare
They are "the next horizon" in healthcare, says Accenture Digital Health Technology Vision 2022 report.
Nathan Eddy
c|net
READY PLAYER ONE!
2011
2021
Will Zuckerberg's 'metaverse' change everything?
Facebook wants to build the VR universe we all live and work in. Here's what's actually coming.
COMPUTERWORLD

Hardware Drivers!
Analytics Insight
INSIGHTS
LATEST NEWS
MAGAZINE
ABOUT US
SUBMIT NEWS
CONNECT
RESOURCES
THE INTEGRATION OF 5G WITH AUGMENTED AND VIRTUAL REALITY
LATEST NEWS
by Priya Dialani February 9, 2020 0 comments
5G
Amazon Promises "single-digit latency" for AR/VR Streaming Over 5G with AWS Wavelength
Image courtesy AWS
By Ben Lang - Jan 28, 2020 21
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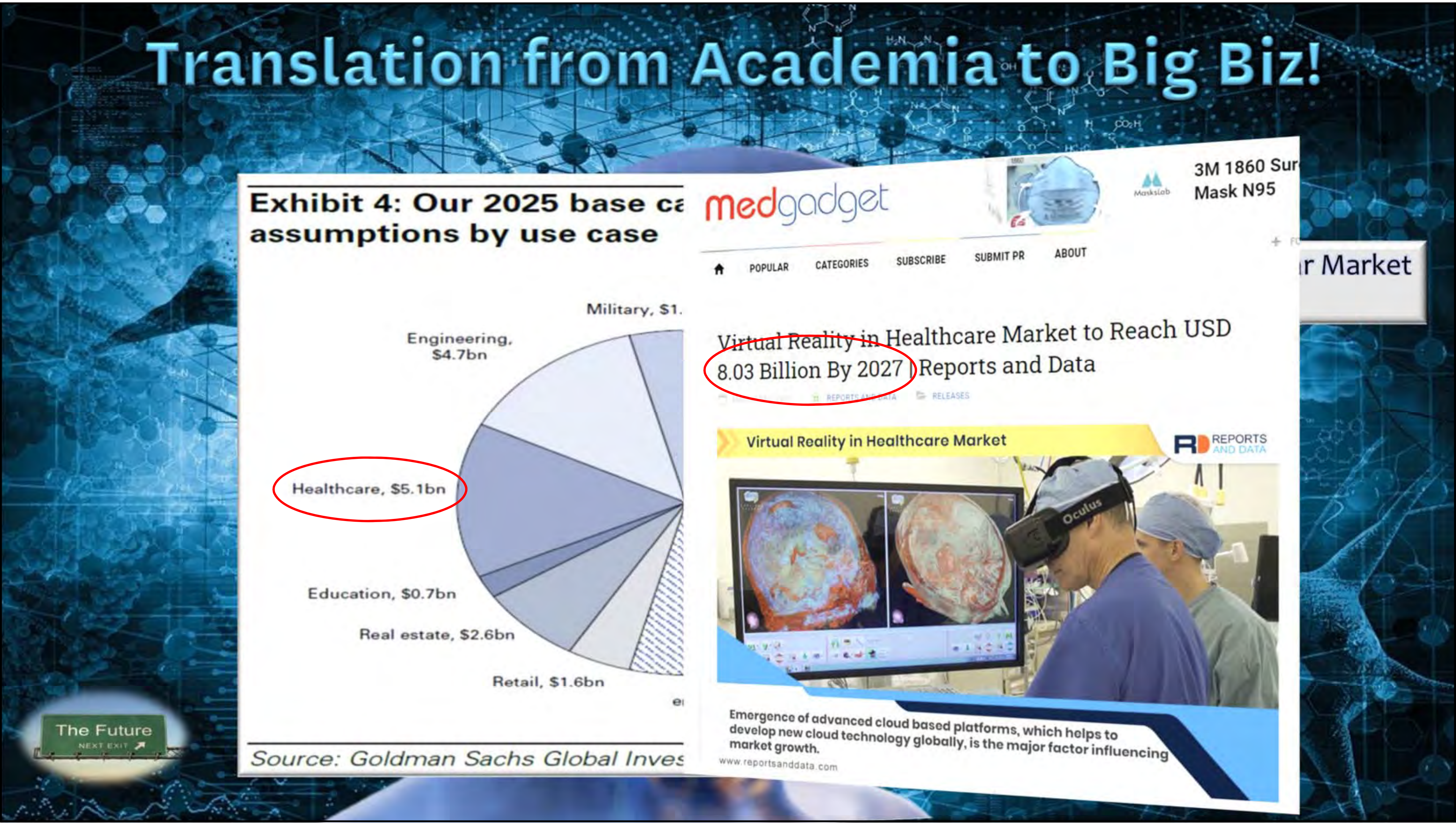
39,829 Fans
13,574 Followers
66,541 Followers
27,600 Subscribers
Last month Amazon quietly announced the 'Wavelength' platform as part of its Amazon Web Services (AWS) offering. The new 'edge computing' service promises "single-digit millisecond latencies" over 5G networks. Amazon says the platform is made for "latency-sensitive workloads" including AR/VR streaming, game streaming, IoT and more.
AWS is one of the most prevalent cloud computing platforms in the world, acting as the back-end web infrastructure for millions of customers.


Translation from Academia to Big Biz!
Exhibit 4: Our 2025 base ca
assumptions by use case
Military, $1.
Engineering, $4.7bn
Healthcare, $5.1bn
Education, $0.7bn
Real estate, $2.6bn
Retail, $1.6bn
Source: Goldman Sachs Global Inves
medgadget
3M 1860 Sur
Mask N95
POPULAR
CATEGORIES
SUBSCRIBE
SUBMIT PR
ABOUT
r Market
Virtual Reality in Healthcare Market to Reach USD 8.03 Billion By 2027 | Reports and Data
Virtual Reality in Healthcare Market
REPORTS AND DATA
Oculus
Emergence of advanced cloud based platforms, which helps to develop new cloud technology globally, is the major factor influencing market growth.
www.reportsanddata.com
The Future
NEXT EXIT


oVRcome
Fearless
Overcome your fears with Virtual Reality.
Limbix
BehaVR
AppliedVR
Virtual reality.
Real change.
XForce
Atmosphaeres
HOME SHOP MORE TECH
Dream Beach 360
Relax like never before
Made for VR
COGNITIVE LEAP
NEURO REHAB VR
PSYTECH
VIRTUAL REALITY ENVIRONMENTS FOR ANXIETY MANAGEMENT
Viva Vita
Live Life
VBI
evolv
TRIPP
unello design
Experiences
virtually free
Penumbra
REAL
MIERON
PSIOUS
The most effective and fast treatment
Virtual reality is a technique which has been
jintronix
GUIDED MEDITATION VR
YOU DESERVE A VACATI
DOWNLOAD OS X
BEHAVR
neo AUVRA BIONICS
CleVR
company info blog forum egx 2015
moving therapy forward moovd
Bright Cloud International
HATSUMI
magic horizons
my better life
root virtual reality
floreo
RECOVR
empowered progress
Relaxing with Perfect Beach
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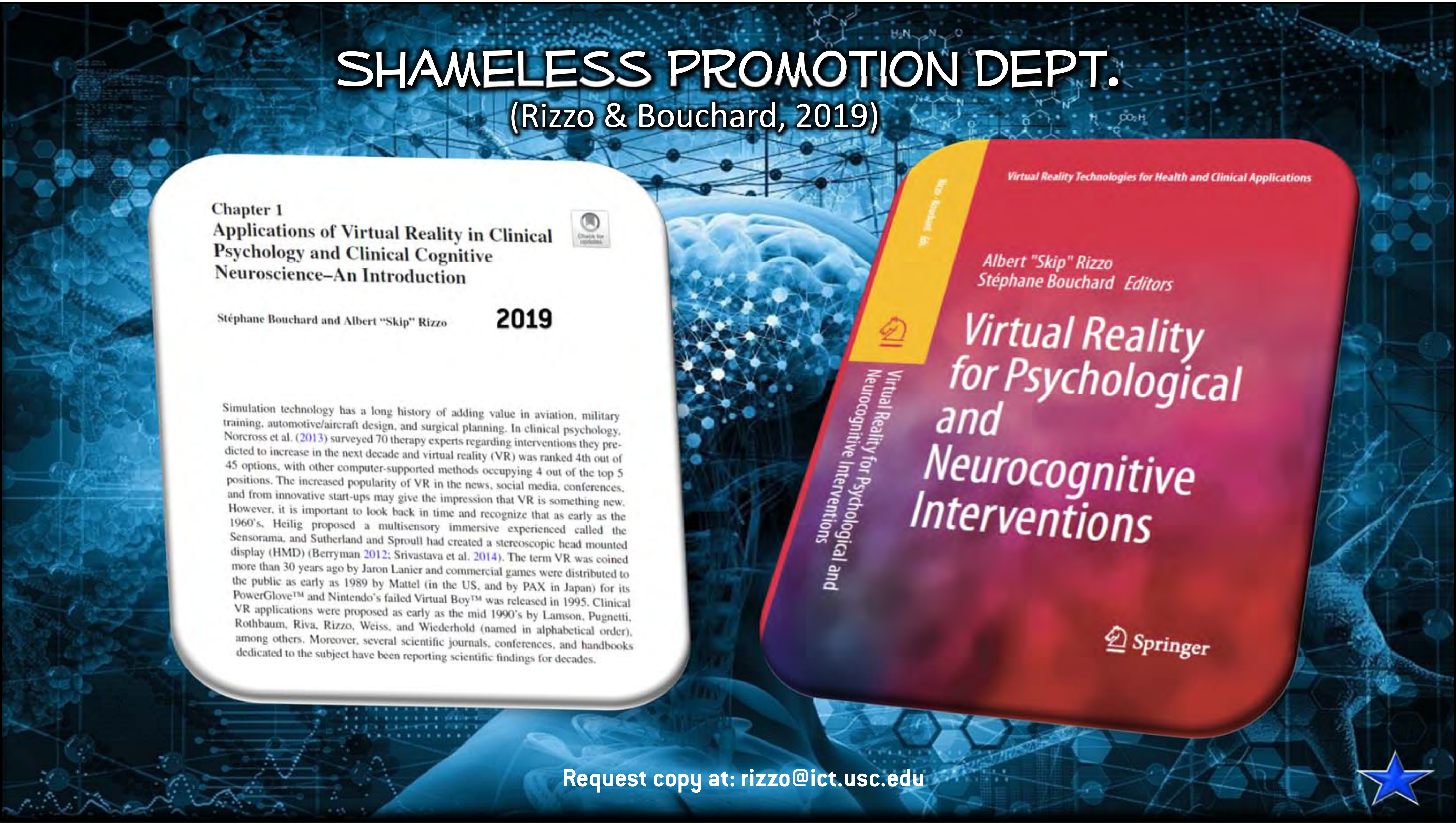
Is VR Dead??
Forbes Leadership Money Business Small Business
2,322 views | May 5, 2020, 04:48am EDT
Stop Saying Virtual Reality Is Dying
Joe Parlock Contributor
Games
I write about the virtual reality industry, VR hardware and its software.
Holi
By Scott Hayden - Dec 30, 2019 2
ps
Image courtesy Oculus


SHAMELESS PROMOTION DEPT.
(Rizzo & Bouchard, 2019)
Chapter 1
Applications of Virtual Reality in Clinical Psychology and Clinical Cognitive Neuroscience–An Introduction
Stéphane Bouchard and Albert "Skip" Rizzo
2019
Simulation technology has a long history of adding value in aviation, military training, automotive/aircraft design, and surgical planning. In clinical psychology, Norcross et al. (2013) surveyed 70 therapy experts regarding interventions they predicted to increase in the next decade and virtual reality (VR) was ranked 4th out of 45 options, with other computer-supported methods occupying 4 out of the top 5 positions. The increased popularity of VR in the news, social media, conferences, and from innovative start-ups may give the impression that VR is something new. However, it is important to look back in time and recognize that as early as the 1960's, Heilig proposed a multisensory immersive experienced called the Sensorama, and Sutherland and Sproull had created a stereoscopic head mounted display (HMD) (Berryman 2012; Srivastava et al. 2014). The term VR was coined more than 30 years ago by Jaron Lanier and commercial games were distributed to the public as early as 1989 by Mattel (in the US, and by PAX in Japan) for its PowerGlove™ and Nintendo's failed Virtual Boy™ was released in 1995. Clinical VR applications were proposed as early as the mid 1990's by Lamson, Pugnetti, Rothbaum, Riva, Rizzo, Weiss, and Wiederhold (named in alphabetical order), among others. Moreover, several scientific journals, conferences, and handbooks dedicated to the subject have been reporting scientific findings for decades.
Virtual Reality Technologies for Health and Clinical Applications
Albert "Skip" Rizzo
Stéphane Bouchard Editors
Virtual Reality for Psychological and Neurocognitive Interventions
Springer
Request copy at: rizzo@ict.usc.edu

FOR THE YOUNG AT HEART

University of Southern California
Russ Shilling, Arno Hartholt, Andrew Leeds, David Kwok, Sharon Mozgai, Jarrell Pair

Long Beach VA
Chris Reist, Todd Adamson

Emory University
Barbara Rothbaum, Tanja Jovanovic, Seth Norrholm, Maryrose Gerardi

Flinders University
Belinda Lange, Sebastian Koenig

MedVR lab

Skip Rizzo, Director

Uniform Services University of the Health Sciences
Michael Roy

Puget Sound VA
Greg Reger, Aaron Norr, Matt Mishkind

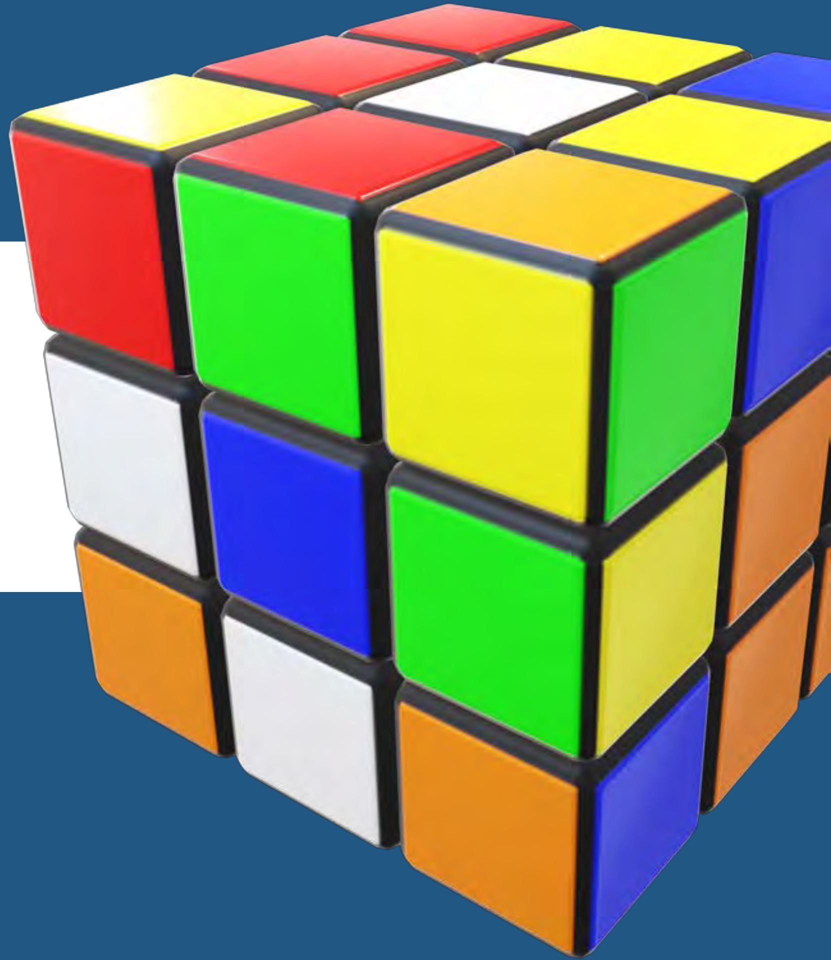
Weill Cornell Graduate School of Medical Sciences
JoAnn Difede, Judith Cukor

Soldier Strong Foundation
Chris Meek

And many others too numerous to name!!

USC Institute for Creative Technologies

Discussion & Questions?



VALGENESIS

Regulatory Framework for the Digital World

27 AUG 2021

Steve Thompson, Director Industry Solutions

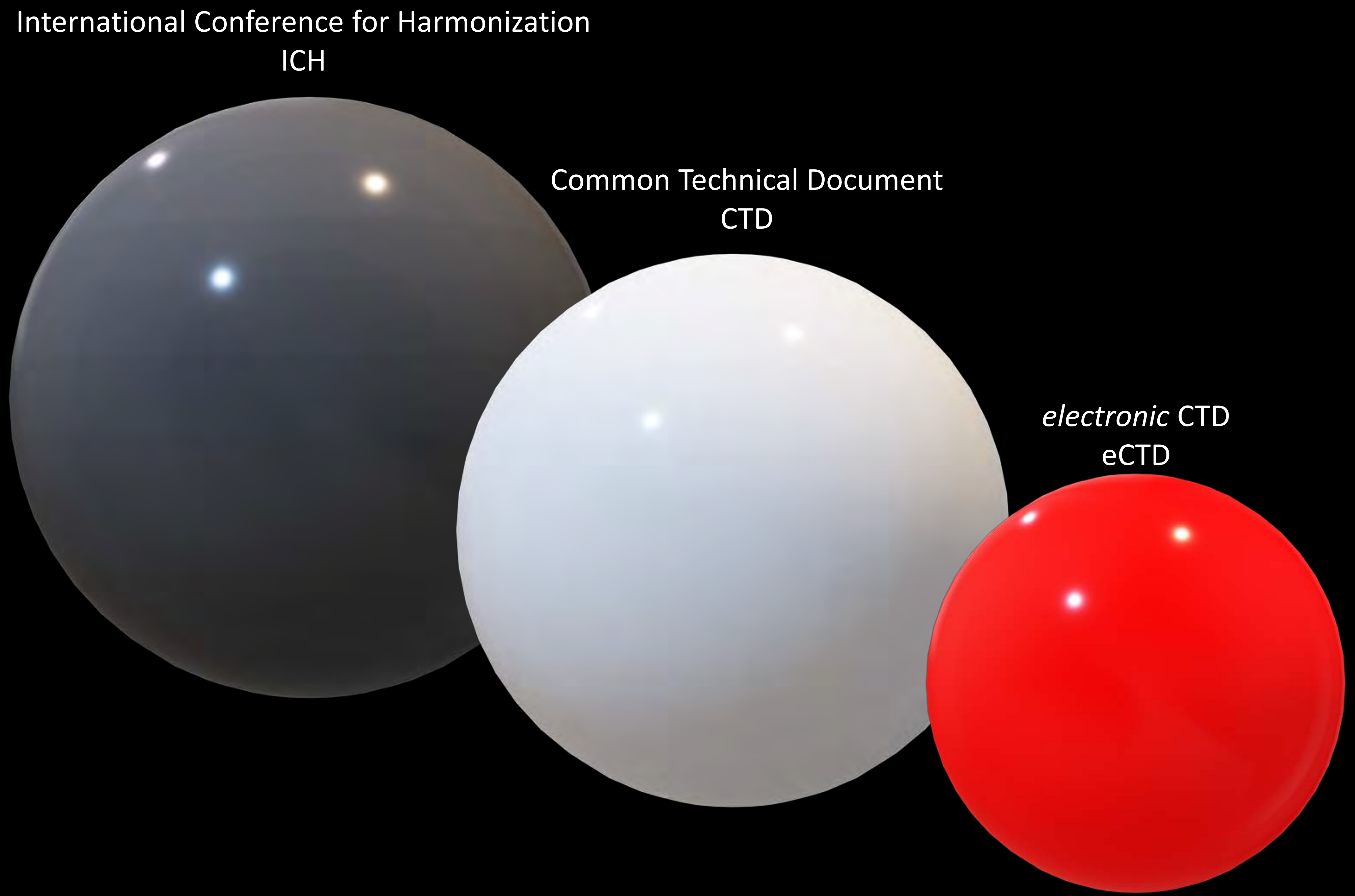
ValGenesis VLMS
The de facto standard for

100%
PAPERLESS
VALIDATION

ValGenesis, Inc., 395 Oyster Point Boulevard, Suite 228, South San Francisco, CA 94080   Phone 510 445 0505

The nice thing about standards is that you have so many to choose from.

Arthur S Tanenbaum

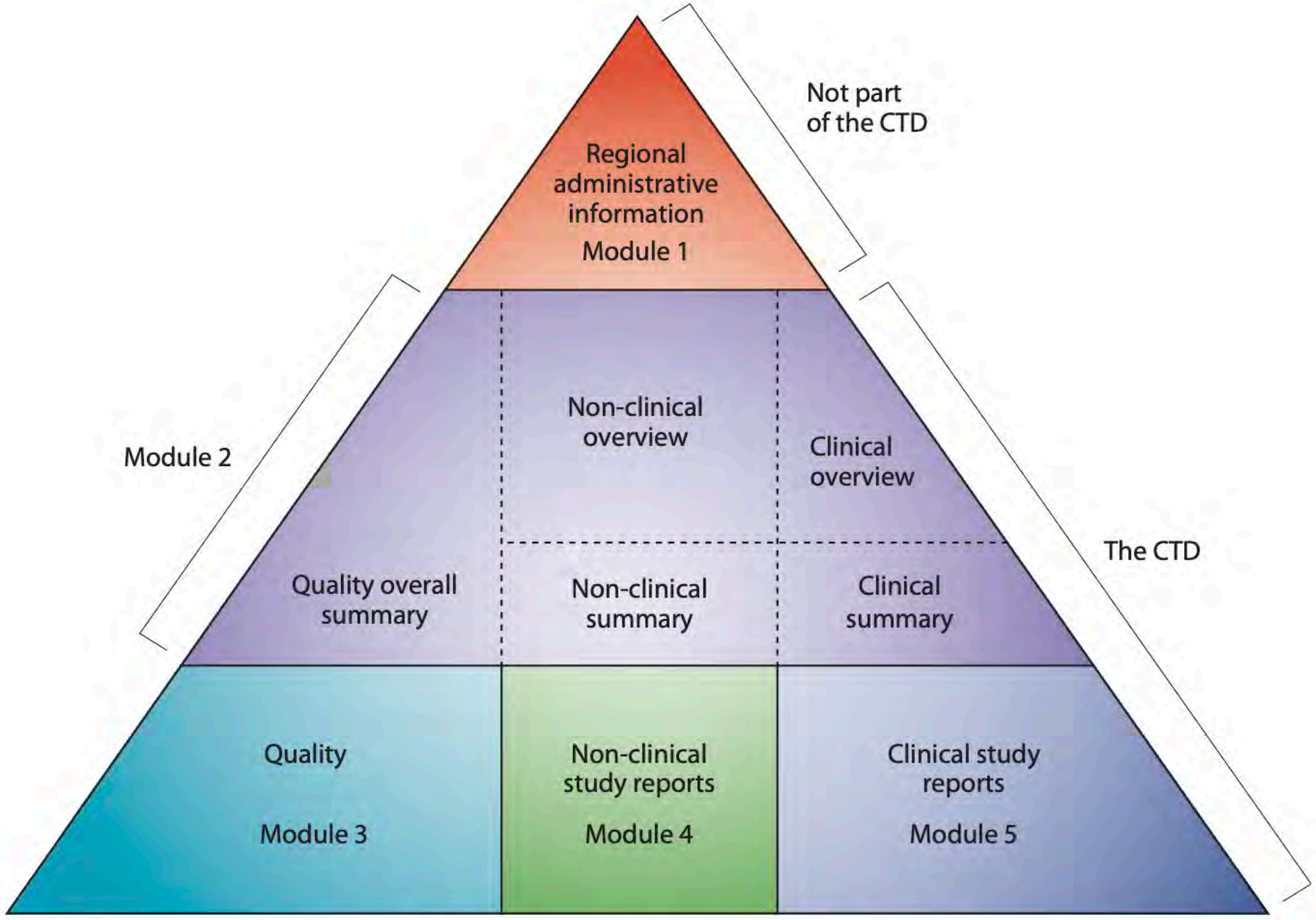

International Conference for Harmonization
ICH
Common Technical Document
CTD
electronic CTD
eCTD

electronic Common Technical Document

eCTD

- An interface and international specification
- Pharmaceutical industry to agency transfer of regulatory information
- Specification is based on the Common Technical Document (CTD)
- Developed by the International Council for Harmoniztion (ICH)
  Multidisciplinary Group 2 Expert Working Group (ICH M2 EWG)

CTD Triangle



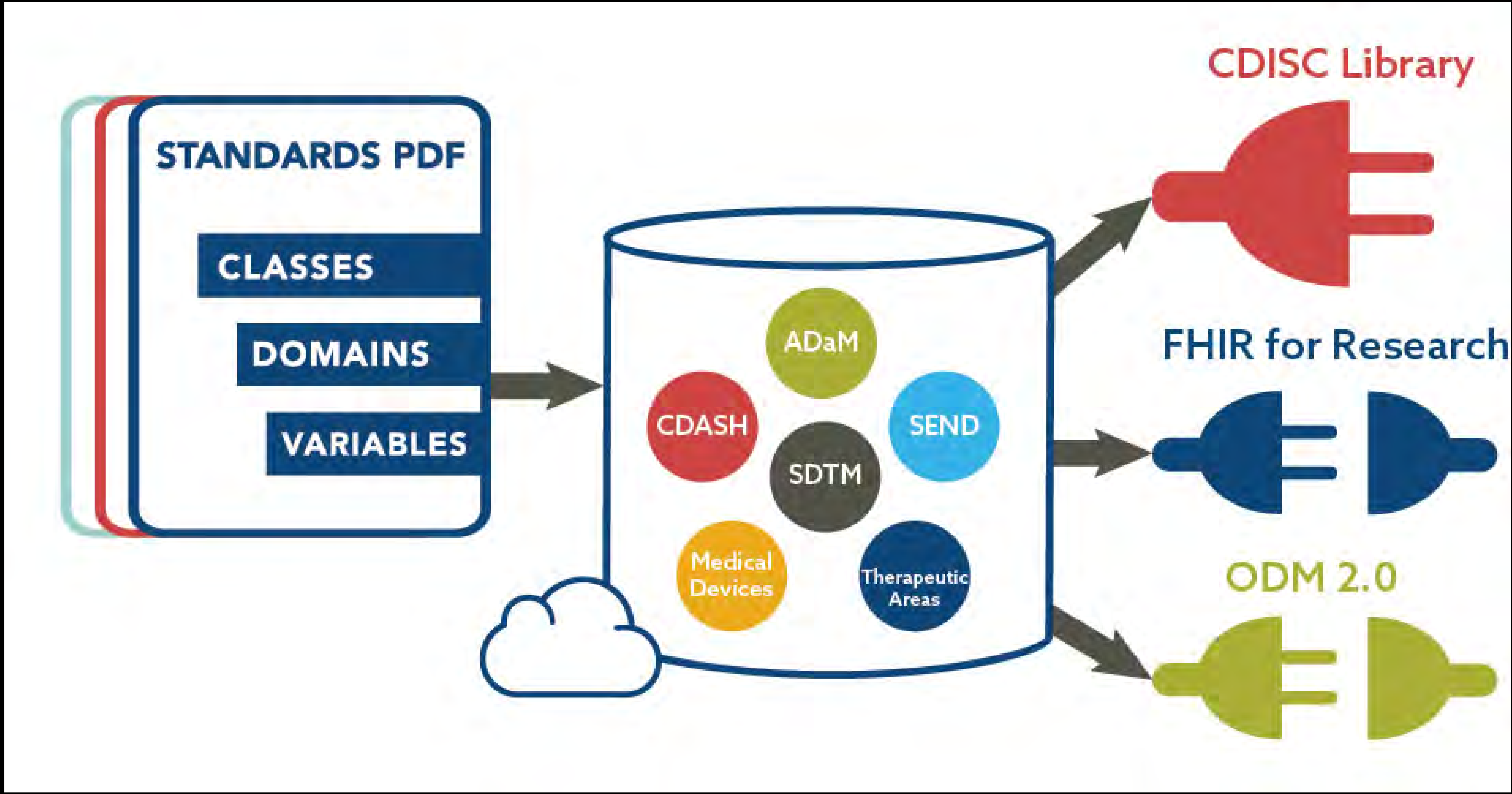
The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

ich.org

Clinical Data Interchange Standards Consortium

cdisc.org

NOTE: “Clinical Data”


STANDARDS PDF
CLASSES
DOMAINS
VARIABLES
ADaM
CDASH
SEND
SDTM
Medical Devices
Therapeutic Areas
CDISC Library
FHIR for Research
ODM 2.0

cdisc.org

HL7 International

Health Level 7

How did HL7 get its name?

Health Level-7 (HL7) was created by Health Level Seven International, a non-profit organization dedicated to developing standards for the exchange of electronic health care data.

```xml
<?xml version="1.0" encoding="UTF-8"?>
<PRPA_IN101001UV01 ITSVersion="XML_1.0" xmlns="urn:hl7-org:v3"
      xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <id extension="3948375" root="2.16.840.1.113883.19.10.700363.2288"/>
  <creationTime value="20060501140010"/>
  <versionCode code="NE2006"/>
  <!-- Interaction is a notification of a person registration -->
  <interactionId extension="PRPA_IN101001UV01" root="2.16.840.1.113883.1.6"/>
  <processingCode code="P"/>
  <processingModeCode code="T"/>
  <acceptAckCode code="ER"/>
  <receiver>
    <device>
    <id extension="922" root="2.16.840.1.113883.19.9"/>
    <name>Master MPI</name>
      <asAgent>
        <representedOrganization>
          <id extension="1002003" root="2.16.840.1.113883.19.200"/>
          <name>Alpha Hospital</name>
        </representedOrganization>
      </asAgent>
    </device>
  </receiver>
  <sender>
    <device>
      <id extension="1" root="2.16.840.1.113883.19.9"/>
    </device>
```

American Standard Code for Information Interchange

ASCII

ASCII Code: Character to Binary

0	0011 0000	O	0100 1111	m	0110 1101
1	0011 0001	P	0101 0000	n	0110 1110
2	0011 0010	Q	0101 0001	o	0110 1111
3	0011 0011	R	0101 0010	p	0111 0000
4	0011 0100	S	0101 0011	q	0111 0001
5	0011 0101	T	0101 0100	r	0111 0010
6	0011 0110	U	0101 0101	s	0111 0011
7	0011 0111	V	0101 0110	t	0111 0100
8	0011 1000	W	0101 0111	u	0111 0101
9	0011 1001	X	0101 1000	v	0111 0110
A	0100 0001	Y	0101 1001	w	0111 0111
B	0100 0010	Z	0101 1010	x	0111 1000
C	0100 0011	a	0110 0001	y	0111 1001
D	0100 0100	b	0110 0010	z	0111 1010
E	0100 0101	c	0110 0011	.	0010 1110
F	0100 0110	d	0110 0100	,	0010 0111
G	0100 0111	e	0110 0101	:	0011 1010
H	0100 1000	f	0110 0110	;	0011 1011
I	0100 1001	g	0110 0111	?	0011 1111
J	0100 1010	h	0110 1000	!	0010 0001
K	0100 1011	i	0110 1001	'	0010 1100
L	0100 1100	j	0110 1010	"	0010 0010
M	0100 1101	k	0110 1011	(	0010 1000
N	0100 1110	l	0110 1100	)	0010 1001
				space	0010 0000

Other standard file formats / protocols

.gif
.jpg / jpeg
.mpg
.mpg4
.png
.doc / docx
.xls / xlsx
.ppt
.pdf

VHS
TCP/IP
XML
HTTP
HTTPS

Technology needs standards

The difference between Frameworks & Standards

- Standard are accepted as best practices whereas framework are practices that are generally employed
- Standard are specific while framework are general

differencebetween.com

A framework is something vague that
provides guidelines on how to do something,
like best practices and you
do not have to follow it.

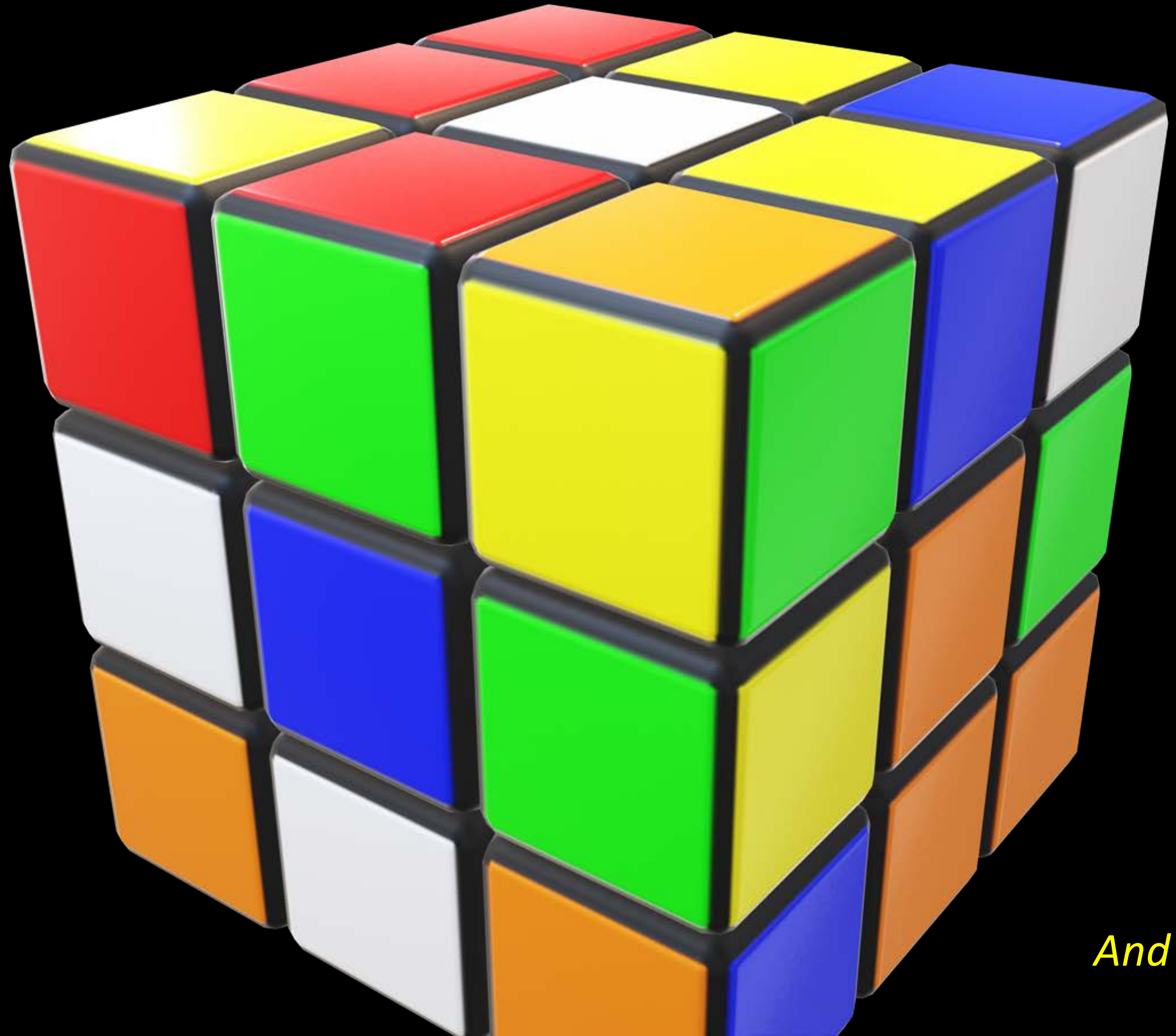
However,
a standard is something that is defined very well and
you have to follow it.

infosecinstitute.com

Regulatory
Frameworks
Standards
Technologies

The problem is we don’t really have **ONE**

The nice thing about standards is that you have so many to choose from.



And we desperately need ONE

So, let’s make one

Taxonomy

tax·on·o·my

/takˈsänəmē/ *

a system of classification

* International Phonetic Alphabet (IPA)

Basic Syllable Rules

To find the number of syllables:
---count the vowels in the word, ...

- Divide between two middle consonants. ...
- Usually divide before a single middle consonant. ...
- Divide before the consonant before an "-le" syllable. ...
- Divide off any compound words, prefixes, suffixes and roots which have vowel sounds.

http://english.glendale.cc.ca.us/phonics.rules.html

Ontology

on·tol·o·gy

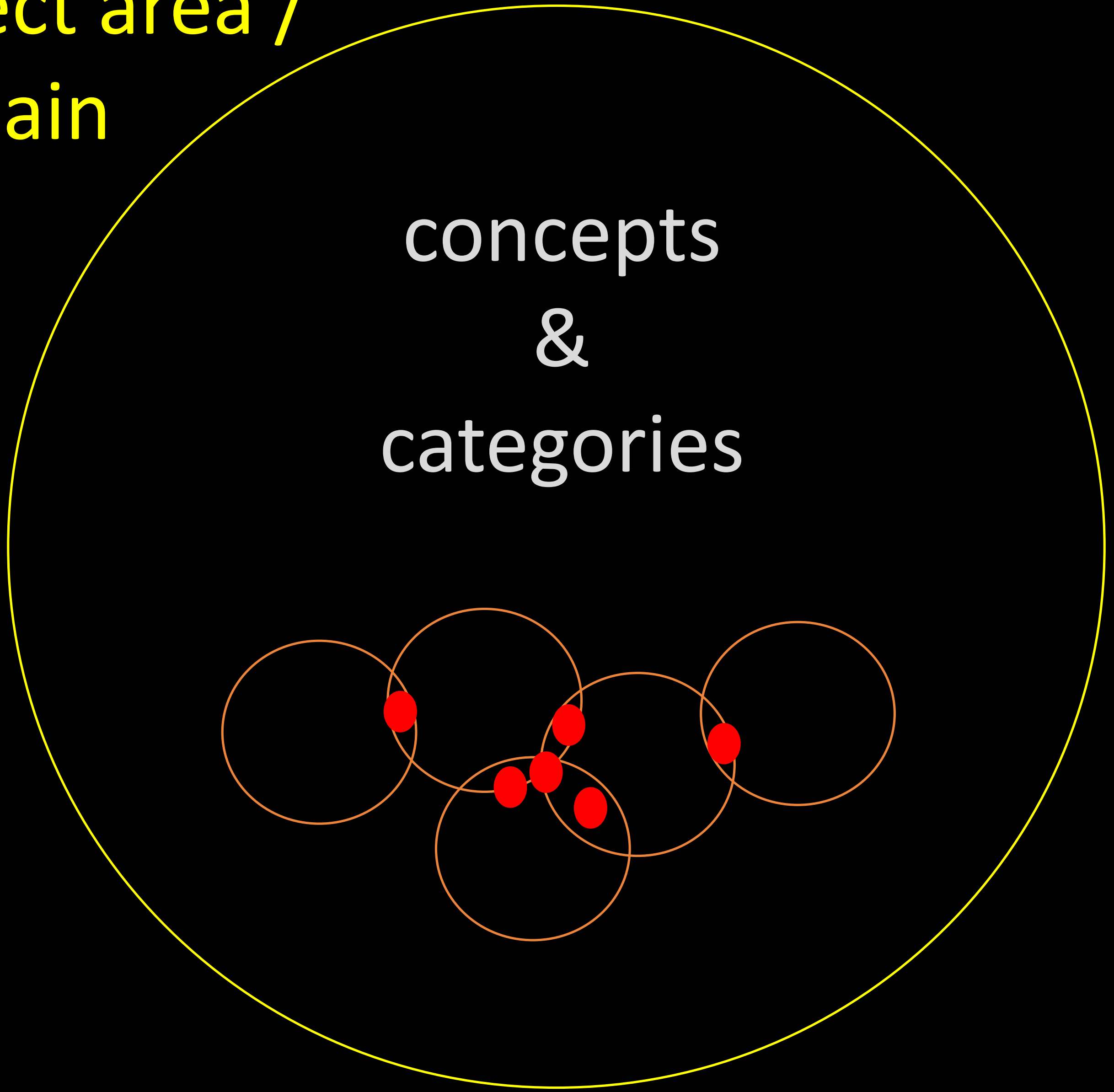
/änˈtäləjē/ *

a set of concepts and categories
in a subject area or domain
that shows their properties
and the relations between them.

* IPA

Ontology

subject area / domain



Dogs → Coat → [Hair | Fur]
Dogs → Tail → hindquarters → [long | short | curly | none]

that shows their properties
and the relations between them.

We desperately need one because…

We're in the 4th Industrial Revolution (Industry 4.0 / Pharma 4.0)

The Fourth Industrial Revolution is

- automation of traditional manufacturing and industrial practices,
- using modern smart technology (AI/ML, IoT, …)

Pharma 4.0™ is an ISPE framework

- adapting digital strategies
- unique contexts of pharmaceutical manufacturing
- especially using more analytical information
- to improve productivity and product quality

We need technology to advance, compete, and survive

Technology needs Standards, that are based on a Framework

We desperately need one because…

Data is a most valued asset
If we can mine data, we can find cures (AI/ML)
Continuous Process Verification
Continuous Validation
Continuous Audit
Virtual Audit / Inspection
Agency Review
Quality by Design
Quality by Review
Reactive > Proactive > Predictive > Prescriptive

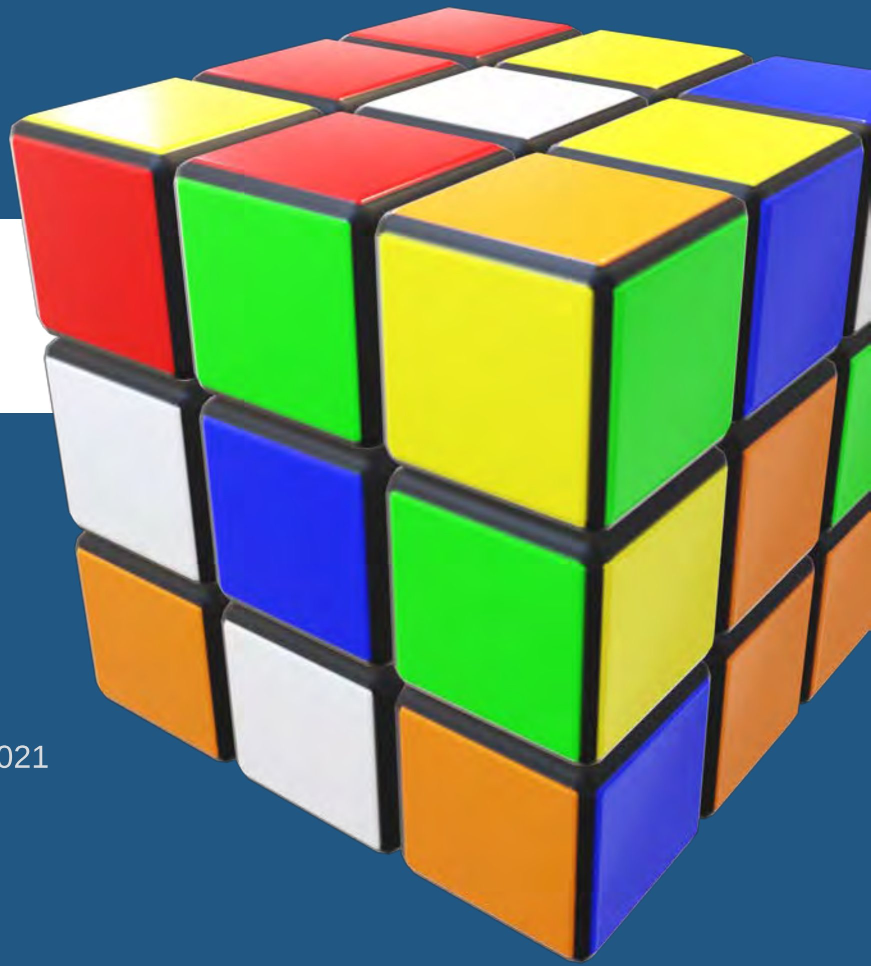
We’ll have to make one

"The person who says it cannot be done should not interrupt the person who is doing it."

- Chinese Proverb

Valgenesis.com

T H A N K   Y O U



Regulatory Framework for the Digital World

27 AUG 2021

Steve Thompson, Director Industry Solutions

Steven.Thompson@valgenesis.com

Mobile
(01) 805-509-4012

AI IN DRUG DEVELOPMENT

MEGAN K. DOYLE, JD, MPH
GLOBAL REGULATORY AND R&D POLICY LEAD,
DIGITAL HEALTH, DIAGNOSTICS, ONCOLOGY

AMGEN®

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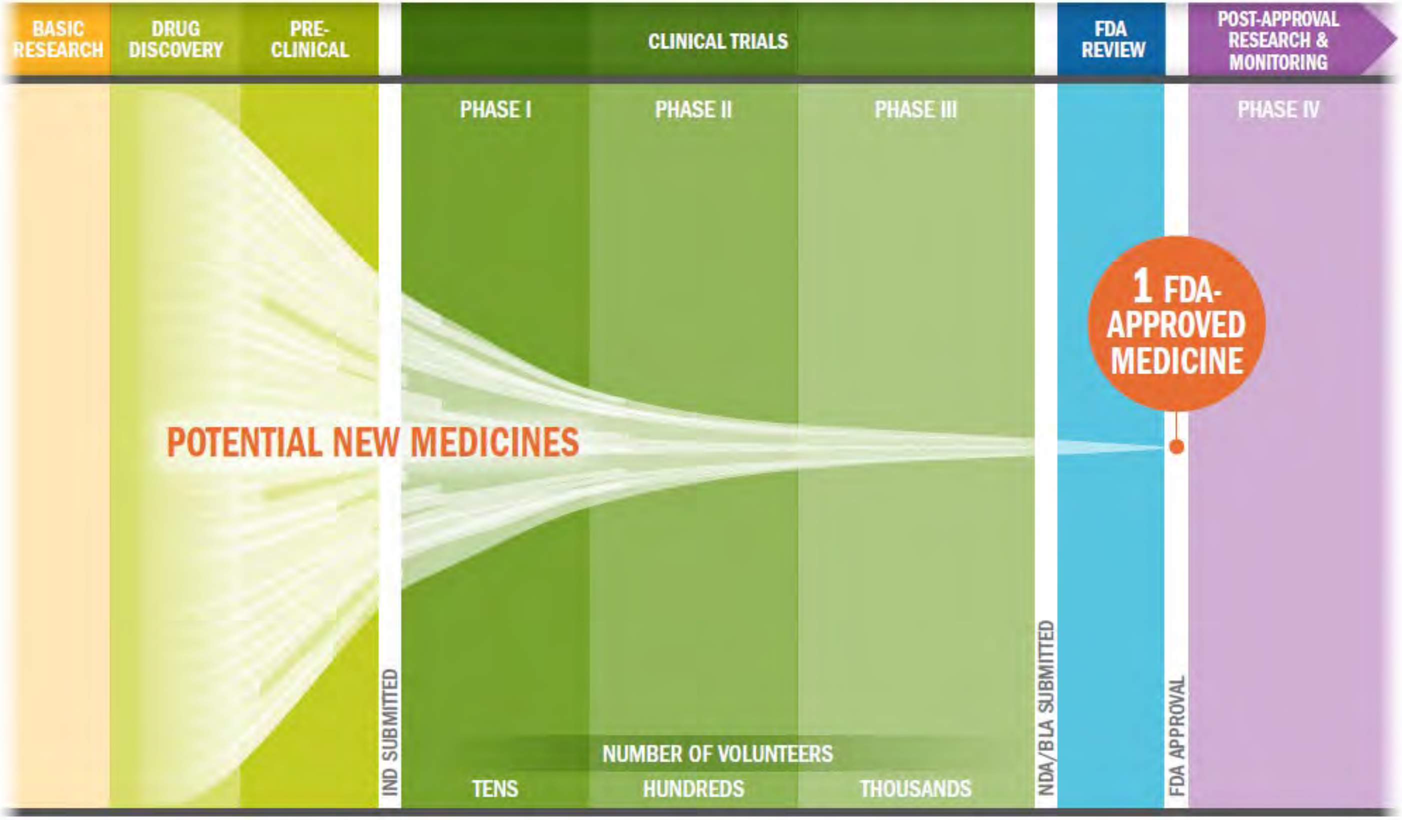
This presentation does not constitute legal advice of any type.

OUTLINE

- Typical drug development process
- Where AI can fit in (premarket, postmarket)
- How AI can fit in – use cases
- Current examples – hot off the press
- Policy issues this raises

TYPICAL DRUG DEVELOPMENT

THE BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT PROCESS



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

Source: PhRMA, Biopharmaceutical Research & Development:The Process Behind New Medicines.

TIMELINE AND COST

Q: How long does it take to bring a new, FDA-approved medicine to patients?

A: At least 10 years, on average.

Source: PhRMA, Biopharmaceutical Research & Development:The Process Behind New Medicines.

TIMELINE AND COST

Q: How much does it cost?

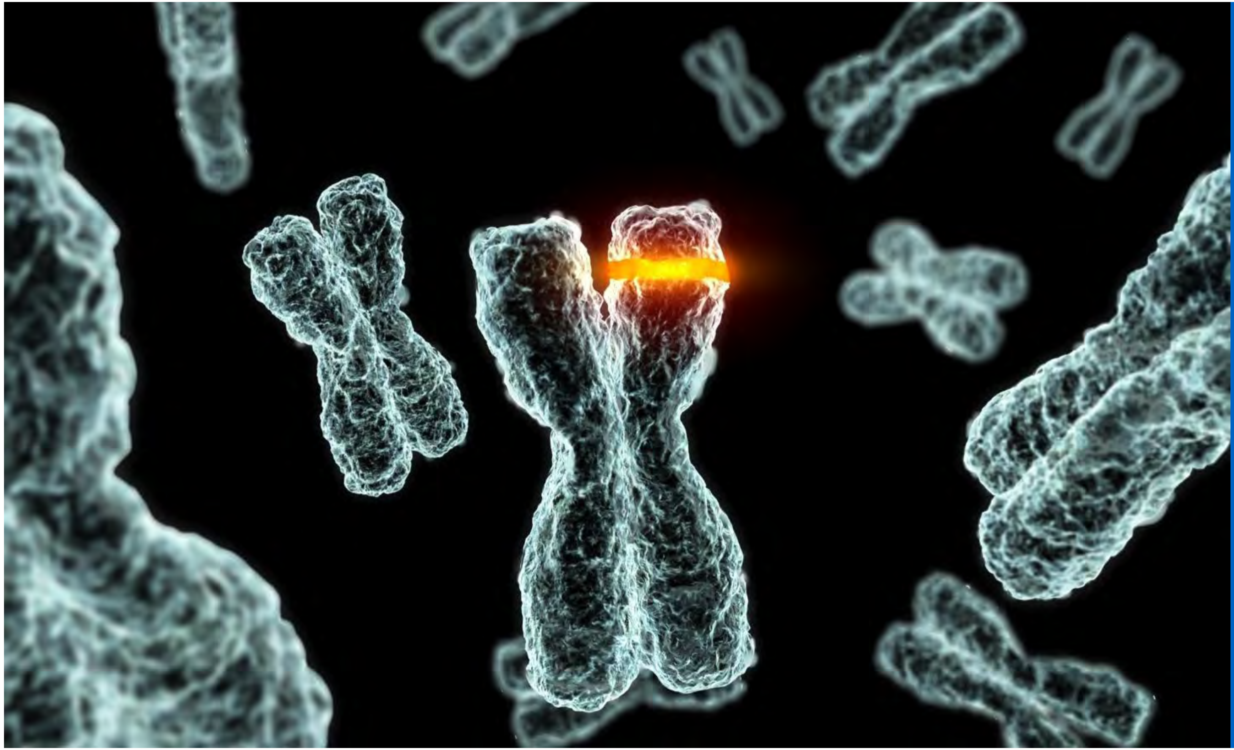
A: $2.6 Billion, on average.

In 2015, the average R&D cost required to bring a new, FDA-approved medicine to patients is estimated to be $2.6 billion over the past decade (in 2013 dollars), including the cost of the many potential medicines that do not make it through to FDA approval.

Source: PhRMA, Biopharmaceutical Research & Development:The Process Behind New Medicines.

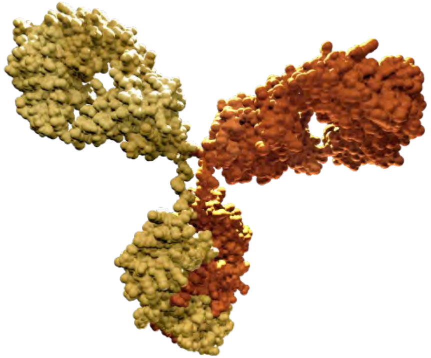
WHERE CAN AI FIT INTO DRUG DEVELOPMENT?

HOW AI CAN FIT IN - PREMARKET

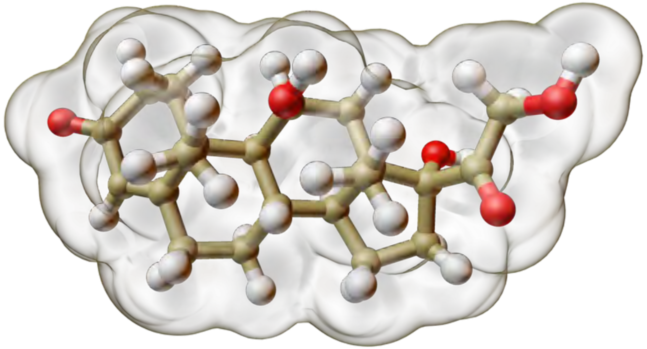


1. Antibody & protein engineering
2. Small molecule design
3. Clinical trial subject identification
4. Clinical trial site selection

HOW AI CAN FIT IN - PREMARKET



Bi-specific antibody



Small molecule

1. Antibody& protein engineering
2. Small molecule design

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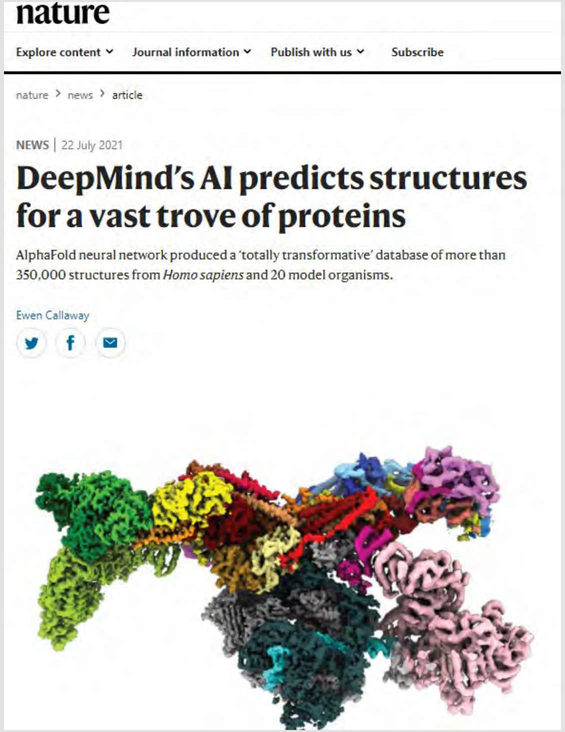
PROTEIN ENGINEERING – USE CASES

Target Discovery	Protein Structure	Protein optimization
• Predict compounds that interact with the target • Predict optimal drug candidate sequences for a protein or target of interest	• Predict protein folding and structure • Some predictions precise enough to detail atomic features useful for drug design • Some tools can compute a prediction in minutes to hours	• Predicting and optimizing properties or protein sequence (properties of a drug compound) • Predict which experiments to conduct to optimize protein, for more efficient drug development

Sources: absi.com/technology, accessed 8/20/21; AI in Drug Discovery Requires Extensive Chemical Libraries, Finds IDTechEx, Aug. 18, 2021; Callaway, E., "DeepMind's AI predicts structures for a vast trove of proteins," Nature | Vol 595 | 29 July 2021 | 635.

Presentation to limited audience on given date. Not intended for further distribution

CURRENT EXAMPLES – HOT OFF THE PRESS



nature

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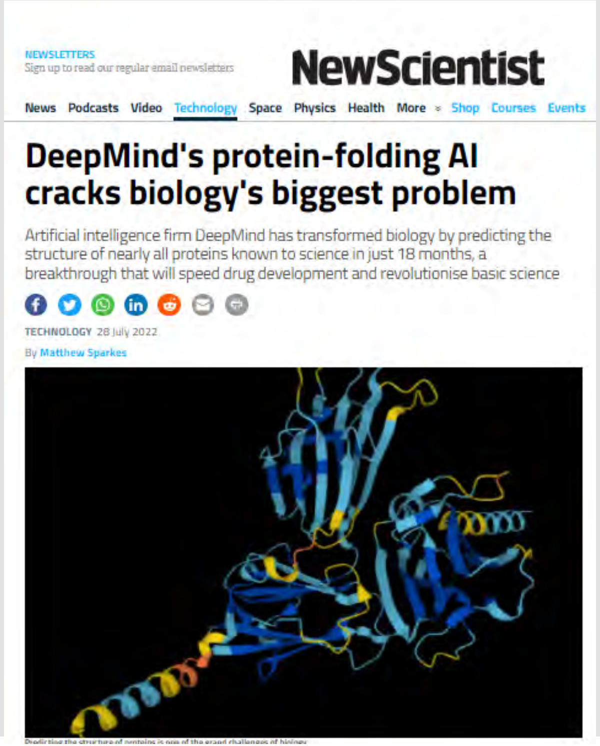
nature > news > article

NEWS | 22 July 2021

DeepMind's AI predicts structures for a vast trove of proteins

AlphaFold neural network produced a 'totally transformative' database of more than 350,000 structures from *Homo sapiens* and 20 model organisms.

Ewen Callaway



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DeepMind's protein-folding AI cracks biology's biggest problem

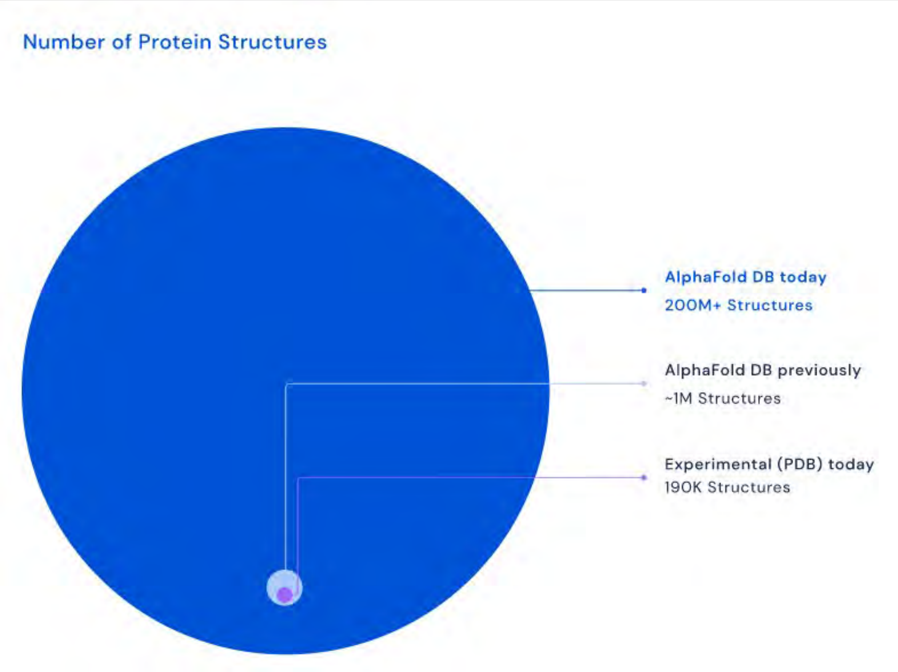
Artificial intelligence firm DeepMind has transformed biology by predicting the structure of nearly all proteins known to science in just 18 months, a breakthrough that will speed drug development and revolutionise basic science

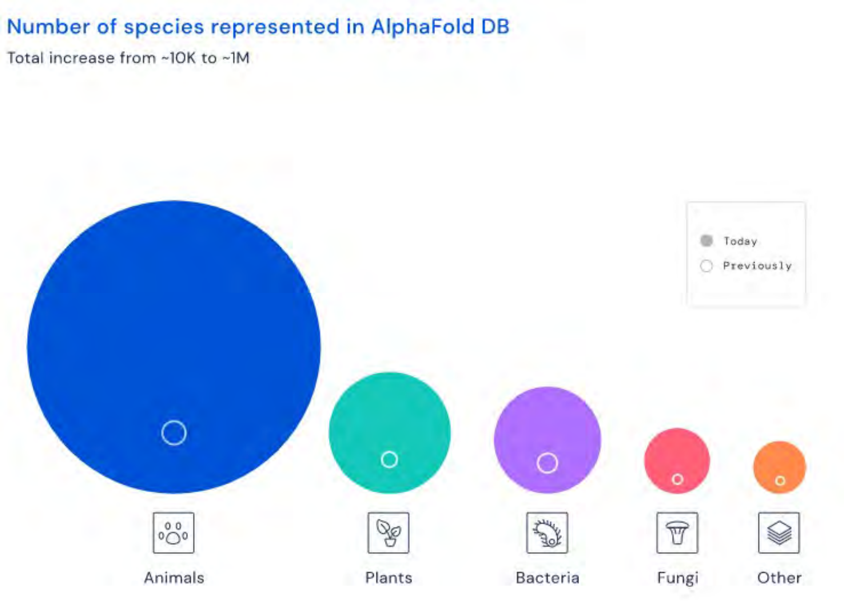
TECHNOLOGY 28 July 2022

By Matthew Sparkes

Sources: Callaway, E., "DeepMind's AI predicts structures for a vast trove of proteins," Nature | Vol 595 | 29 July 2021 | 635; Sparkes, M., "DeepMind's protein-folding AI cracks biology's biggest problem," NewScientist, 28 July 2022.

CURRENT EXAMPLES – HOT OFF THE PRESS





Sources: DeepMind, Inc, Press Release: [AlphaFold reveals the structure of the protein universe](), 28 July 2022.
.

CURRENT EXAMPLES – HOT OFF THE PRESS

HOME / PHARMA MANUFACTURING NEWS / BIOPHARMA NEWS /

Healx partners with Ono Pharmaceutical to expand AI capabilities for rare diseases

5 AUGUST 2021 15:05

Drug discovery biotech Healx will work with Ono Pharmaceutical on a project to identify new disease indications with high unmet needs.

Biotech Absci sees shares soar in IPO debut

By Jane Byrne
27-Jul-2021 - Last updated on 27-Jul-2021 at 20:19 GMT


© GettyImages/metamorworks

Source: Byrne J., BioPharma-reporter.com, July 27, 2021; European Pharmaceutical Manufacturer, August 5, 2021.

Presentation to limited audience on given date. Not intended for further distribution.

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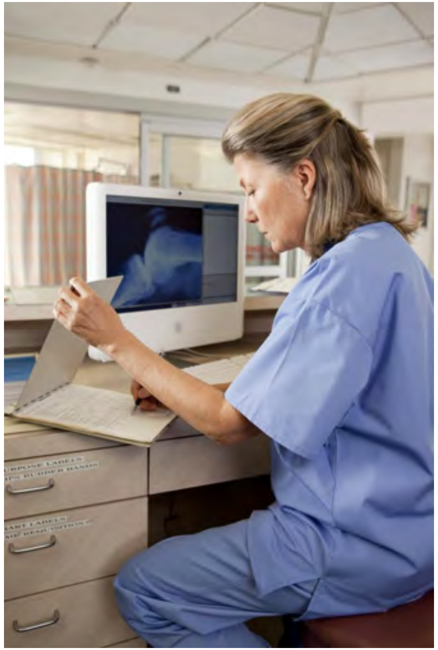
HOW AI CAN FIT IN - PREMARKET



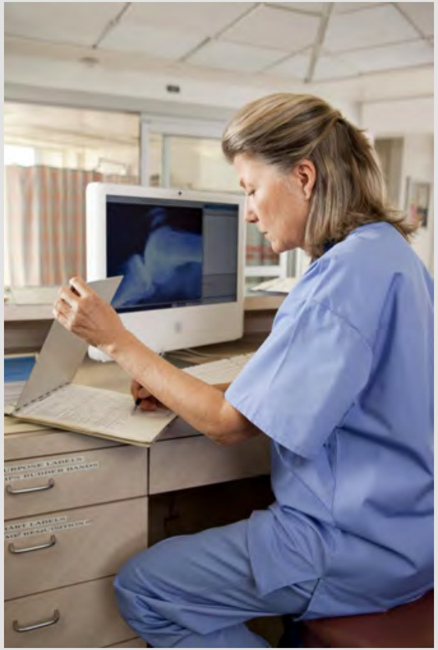
Subject screening

Predicting optimal sites

3. Clinical trial subject identification
4. Clinical trial site selection

AMGEN

CLINICAL TRIALS – USE CASES



- Roughly 80% of clinical trials fail to meet enrollment timelines, and around one-third of Phase III clinical studies are terminated because of enrollment difficulties.
- Subject recruitment tactics historically relied on time-consuming chart reviews by staff, physician referrals, recruitment ads (radio, print, web, etc.)
- Extracting information from medical records — including EHRs and molecular lab test results — is a sought after application of AI.
- Natural language processing (NLP) can help extract and analyze relevant information from EHRs, compare with eligibility criteria, and match patients to trials.
- AI can also be used to create synthetic control arms, identify optimal sites and investigators for recruitment, as well as optimal sites for GCP compliance (based on historical clinical trial data).

Sources: CBInsights, The Future Of Clinical Trials: How AI, Big Tech, & Covid-19 Could Make Drug Development Cheaper, Faster, & More Effective, April 6, 2021; Medidata, AcornAI, accessed 8.20.2021.

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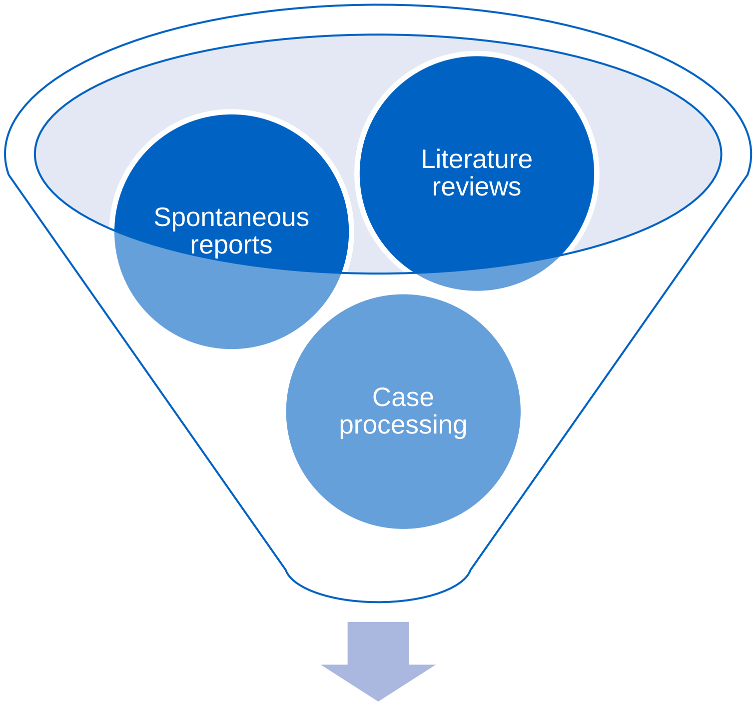
WHERE AI CAN FIT IN – POSTMARKET

- Pharmacovigilance
- Identification of missed or potential patients

HOW AI CAN FIT IN - PHARMACOVIGILANCE



Signal Detection Assessment

Sources: Bhangale, R et al., A Day in the Life of a Pharmacovigilance Case Processor, Perspect Clin Res. 2017 Oct-Dec; 8(4): 192–195.; Murali, K et al., Artificial intelligence in pharmacovigilance: Practical utility, Indian J Pharmacol. 2019 Nov-Dec; 51(6): 373–376.

HOW CAN AI FIT IN – POSTMARKET USE CASES

Case Management	Signal Detection	Patient Identification
• Rule-based algorithm for literature reviews • Rule-based algorithm that identifies spontaneous reports from HCPs	• Algorithm to predict whether evidence exists to support a causal association	• Algorithm aids in diagnosis • Aids in identification of patients in need of an already marketed intervention or therapy

Sources: Bhangale, R et al., A Day in the Life of a Pharmacovigilance Case Processor, Perspect Clin Res. 2017 Oct-Dec; 8(4): 192–195.; Murali, K et al., Artificial intelligence in pharmacovigilance: Practical utility, Indian J Pharmacol. 2019 Nov-Dec; 51(6): 373–376; FDA, Evaluation of Automatic Class III Designation for ContaCT: Decision Summary, 2/13/2018..

CURRENT EXAMPLES – HOT OFF THE PRESS

FDA NEWS RELEASE

FDA Authorizes Marketing of Diagnostic Aid for Autism Spectrum Disorder

Share | Tweet | Linkedin | Email | Print

For Immediate Release: June 02, 2021

Today, the U.S. Food and Drug Administration author
diagnose autism spectrum disorder (ASD). The Cognoa
learning-based software intended to help health care p
18 months through 5 years of age who exhibit potentia

FDA NEWS RELEASE

FDA permits marketing of clinical decision support software for alerting providers of a potential stroke in patients

Share | Tweet | Linkedin | Email | Print

ruary 13, 2018

Drug Administration permitted marketing of the Viz.AI Contact
ical decision support software designed to analyze computed
that may notify providers of a potential stroke in their patients.

FDA NEWS RELEASE

FDA Authorizes Marketing of First Device that Uses Artificial Intelligence to Help Detect Potential Signs of Colon Cancer

Medical device aids clinicians in detecting potential irregularities during colon cancer screening and surveillance

Share | Tweet | Linkedin | Email | Print

For Immediate Release: April 09, 2021

Today, the U.S. Food and Drug Administration authorized marketing of the GI Genius, the first device that uses artificial intelligence (AI) based on machine learning to assist clinicians in detecting lesions (such as polyps or suspected tumors) in the colon in real time during a colonoscopy.

Sources: FDA, News Release, 6/2/21; FDA News Release, 2/13/18; FDA, News Release, 4/9/21.

POLICY ISSUES RAISED BY AI IN DRUG DEVELOPMENT

POLICY ISSUES

Privacy	Regulatory	R&D
• Access to genomic data • Privacy laws – striking the right balance	• US Device regulatory model does not fit AI • AI Regulation in EU not sector specific • What is a diagnostic?	• Which activities are regulated? • Replacing human involvement

AMGEN®

POLICY ISSUES

US

- No national privacy law
- State laws in response – patchwork of requirements
- Device regulatory model must adapt
- What is a diagnostic? What is a companion diagnostic?

EU

- TEHDAS – how to create health data space that enables research
- AI Regulation – how to regulate without impeding AI in drug development
- GDPR – how to protect privacy without inhibiting R&D

REGULATORY POLICY ISSUES, IN DETAIL

"The FDA's traditional paradigm of medical device regulation was not designed for adaptive artificial intelligence and machine learning technologies."

Source: FDA, Artificial Intelligence/Machine Learning-Based Software as a Medical Device Action Plan, January 2021.

REGULATORY POLICY ISSUES, IN DETAIL

- Proposed framework for regulation of AI in Europe
- Not sector-specific: Applies to tech companies, health care, etc.
- Risk-based approach to classification of AI
- Before placing high-risk AI on EU market, must demonstrate system confirms with new mandatory requirements

EUROPEAN COMMISSION

Brussels, 21.4.2021
COM(2021) 206 final

2021/0106 (COD)

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

LAYING DOWN HARMONISED RULES ON ARTIFICIAL INTELLIGENCE (ARTIFICIAL INTELLIGENCE ACT) AND AMENDING CERTAIN UNION LEGISLATIVE ACTS

Source: European Commission, Proposal for a Regulation of the European Parliament and of the Council Laying Down Harmonised Rules on AI, April 2021.

Presentation to limited audience on given date. Not intended for further distribution.

AMGEN®

REGULATORY POLICY ISSUES, IN DETAIL

What is an in vitro diagnostic product (IVD)?

Definition: In vitro diagnostic products are those reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. [21 CFR 809.3]

Regulatory Authority: IVDs are *devices* as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act, and may also be *biological products* subject to section 351 of the Public Health Service Act. Like other medical devices, IVDs are subject to premarket and postmarket controls. IVDs are generally also subject to categorization under the Clinical Laboratory Improvement Amendments (CLIA '88) of 1988.

Companion Diagnostics

Share | Tweet | Linkedin | Email | Print

A companion diagnostic is a medical device, often an in vitro device, which provides information that is essential for the safe and effective use of a corresponding drug or biological product. The test helps a health care professional determine whether a particular therapeutic product's benefits to patients will outweigh any potential serious side effects or risks.

Companion diagnostics can:

- identify patients who are most likely to benefit from a particular therapeutic product;

L 117/178 | EN | Official Journal of the European Union | 5.5.2017

(17) It is necessary to clarify that software in its own right, when specifically intended by the manufacturer to be used for one or more of the medical purposes set out in the definition of an *in vitro* diagnostic medical device, qualifies as an *in vitro* diagnostic medical device, while software for general purposes, even when used in a healthcare setting, or software intended for well-being purposes is not an *in vitro* diagnostic medical device. The qualification of software, either as a device or an accessory, is independent of the software's location or the type of interconnection between the software and a device.

CONCLUSIONS

SUMMARY

- AI has many potential uses in drug development
- Such uses could speed discovery and development of novel therapies
- AI products could also render efficiencies in the postmarket setting and identify patients for therapy
- Privacy and regulatory schemes are trying to adapt, but questions and concerns remain

Securing Emerging Technologies

Jay Nayar, RAC
Google

Agenda

Why

Why is there a demand?

What

What are the expectations?

How

How do we implement to those expectations?

Why

92%

say convenience is an important factor when choosing their primary care provider [3]

CVS study

Market Demand

Research

Real World Evidence[1]

Decentralized Trials[2]

Empower

Convenience[3]

Personalization

Cost-effectiveness

Screening Apps and POC tests[4]

Scale

Health Record[5]

Interoperability

IoT &OTS devices

Cloud based services

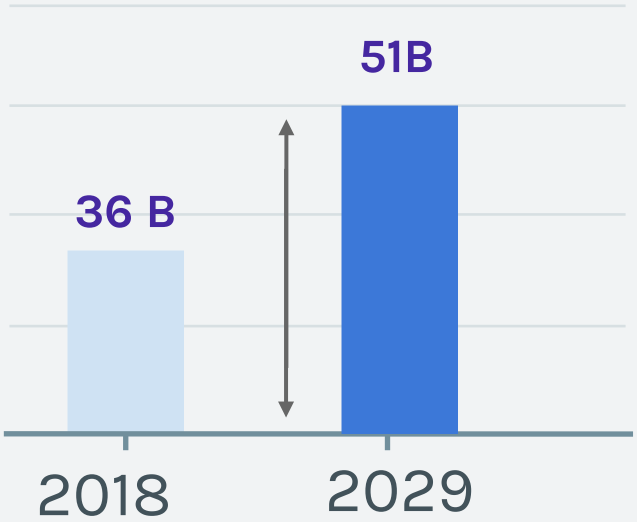
SaaS (AI + Storage)

Market Need:
Connectivity & Personalization

Major increase to consumer demand.

- **64.3% increase** (forecasted) in telehealth demand, 2020[8]
- **40%** of Providers find digital tools valuable for communication[9]
- **83% of Providers** find patient understanding of test results impacts **engagement** [9]

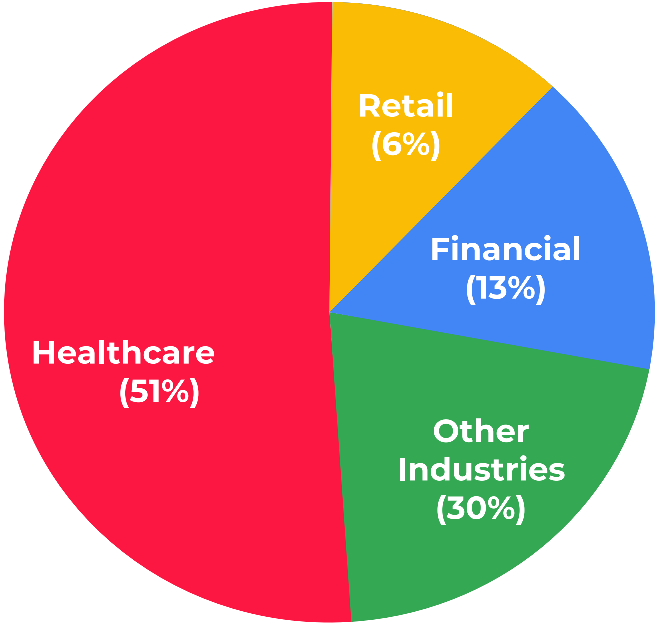
Market Growth:
Point of Care Dx



Global Market[10]

(pre-COVID analysis)

Breach (Ball) Trends



Source: Consumer Identity Breach Report

Research Takeaways

- PII is the highest value to threats[11,16]
- Usage of unsupported OS[14]
- Increasing vulnerable IoT usage[12]
- Mixed asset management leads to malware spread[13]

Regulatory Reaction

- Increased Regulatory controls (CCPA, SB-327)[15]
- Increased cost per Healthcare breach, (~ $7M)[16]
- >40% of executives promise a focus on security[13]
- Even the NSA is interested[17]

Industry and Regulators

//

“Consumers are ***demanding convenience*** *and ease in how they access health services. Technological solutions have the power to simplify health care...”*

Larry Merlo
CEO, CVS Health

“All medical devices that use software and are connected to hospital and health care organizations’ networks ***have vulnerabilities*** *…”*

Suzanne Schwartz,
Director, Office of Strategic Partnerships and Technology Innovation, FDA

Takeaway

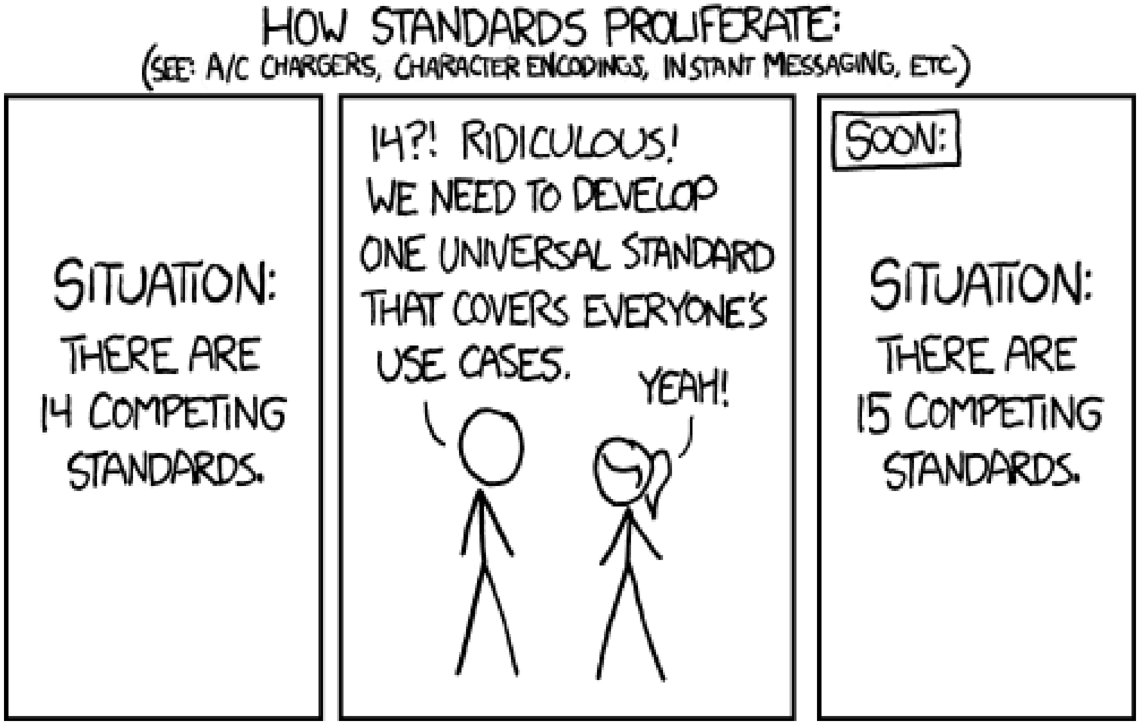
Security is now a market and brand need.

“Security is baked into the DNA of every product.”

“Protecting your privacy starts with the world’s most advanced security.”

“Apple designs security into the core of its platforms.”

What

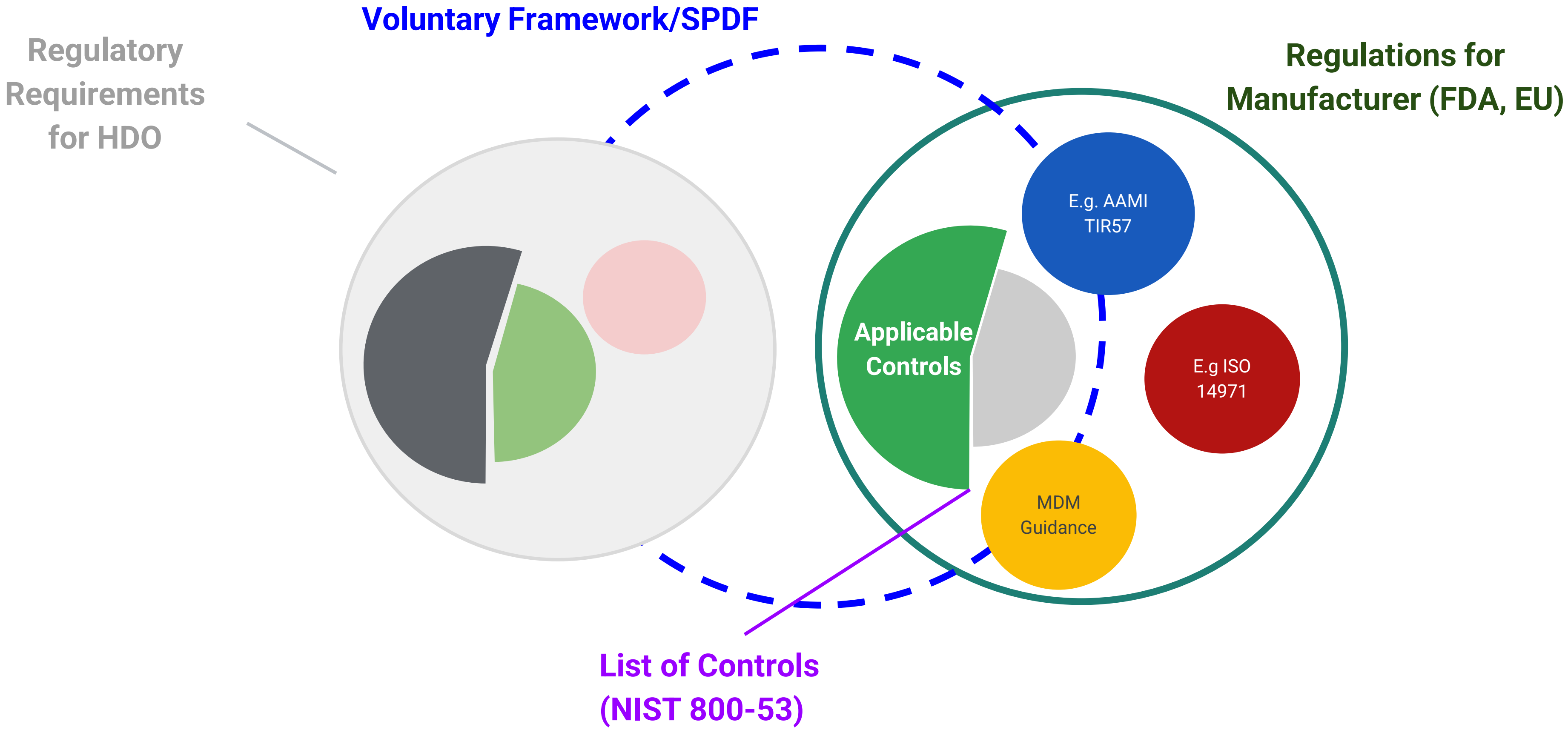


Source:xkcd/standards

What are *not* expectations

- Slow updates
- Poor User Experience
- Regulations and Procedures
- Lack of Expertise
- Inherent Vulnerabilities

Frameworks vs Standards vs Regulations



Framework: Joint Security Plan[22]

What is it?

A voluntary framework for healthcare security. Created by the Healthcare Sector Coordinating Council and endorsed by FDA, device manufacturers , and Hospitals

Why use it?

Comprehensive organizational maturity check.

Recommended FDA expectation (See SPDF requirement in draft guidance)

Referenced by OUS guidance

How to use it?

Standards: IEC 80001 Series

What is it?

Comprehensive set of adaptable standards

Applicable to all Medical Device Manufacturers

Why use it?

HDOs (US) require MDS2 form for connected platforms[23]

Referenced by MDR (MDCG 2019-16) other standards such as IEC 82304-1 and UL 2900-2[24]

How to use it?

Maps all 19 capabilities to technical standards for implementation

Repeatable practice for product development.

Security Capabilities

IEC 80001-2-2

- Auto Log Off
- Audit Controls
- Authorization
- Configuration of Security Features
- Cyber Security Product Upgrades
- Health Data de-identification
- Data Backup and Disaster Recovery
- Emergency Access
- Health Data integrity and Authenticity
- Malware Detection/ Protection
- Node Authentication
- Person Authentication
- Physical Locks on Device
- Third Party components in product lifecycle roadmaps
- System and Application Hardening
- Security Guides
- Health Data Storage Confidentiality
- Transmission Confidentiality
- Transmission Integrity

IEC 80001-2-8

Maps capabilities to sections from NIST/ IEC

Technical

NIST 800-53
- **Benchmark!**
- US Federally recommended Security Controls geared toward organizations
- Highest rigor, acceptability and flexibility
- Use for Med Device Dev by having capability to meet Organizational Security Control

ISO IEC 15408-2
- Security Techniques
- Customized security requirements when no predefined components exist

ISO IEC 15408 - 3
Security Assurance evaluation

IEC 62443-3- Industrial Comm systems
Use for emplaced systems

Operational/Admin

ISO IEC 27002 - Code of Practice
- Organizational practices
- Useful for data handling

ISO 27799 - Health Informatics
Organizational practices for custodians of health data

Standards: AAMI TIR 57

What is it?

- Medical Device specific security **risk management** standard that emulates 14971

Why use it?

- FDA recognized and familiar design
- Enables separation of security and safety domains

How to use it?

- Use to interface safety risks to security root causes
- Develop holistic risk management plans with acceptance criteria for security risks

Guidance: MDCG 2019-16 Guidance

Impact: High

- Traces to MDR GSPR sections
- Min IT requirements
- User group focus
- Security capabilities identical to 80001-2

Status: Final

- Use for Technical Documents
- Upcoming IMDRF guide[25]
- ENISA and EU Cybersecurity Law impact
- Prescriptive tables for risk

Guidance: FDA’s cybersecurity guidance

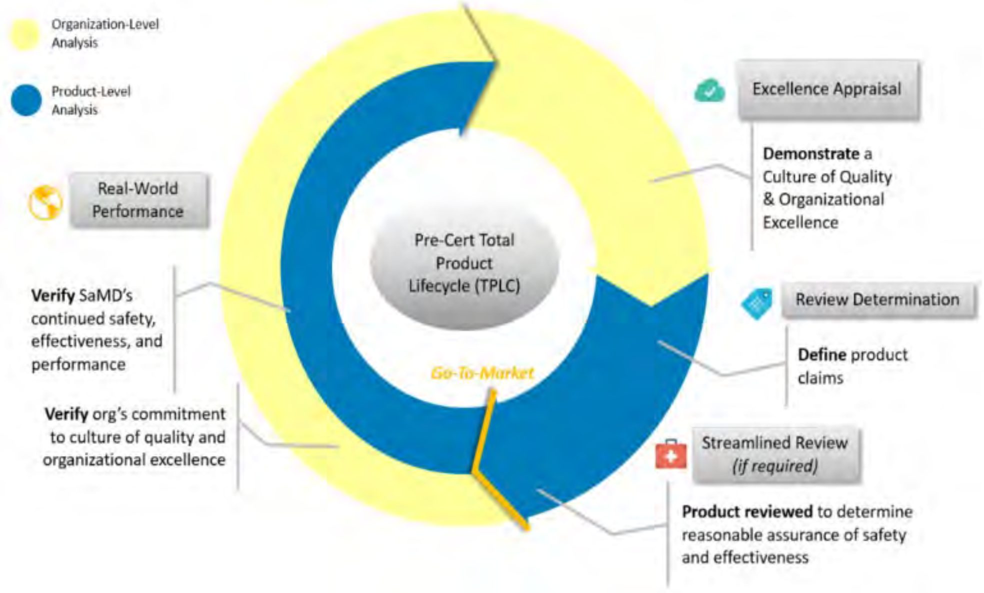
Impact: Medium

- Highlights Framework (SPDF)
- Improved Security Architecture and harm guidance
- Security Controls
- Transparent Communication

Status: Draft

- Updated significantly from earlier draft
- More aligned with JSP and pre-cert.
- Removes tiering
- Reference for current submissions

FDA's future plan: FDA Software Pre-Cert Pilot[26]



Excellence Principles

- Product Quality
- Patient Safety
- Clinical Responsibility
- Cybersecurity Responsibility
- Proactive Culture

Components

- Excellence Appraisal
- Review Determination
- Streamlined Review (if required)
- Real World Performance

FDA's future plan: FDA Software Pre-Cert Pilot

Security Impact:

- Key Excellence Principle
- Streamlined Review component
  - Threat Model
- Real World Performance component
  - Product Performance Analytic (PPA)
- Leverages currently recognized standards, e.g: NIST CSF

Status:

- Build and iterate mode[27]
- Development of libraries and metrics [28]
- Understanding product measures that correlate to performance[28]

How

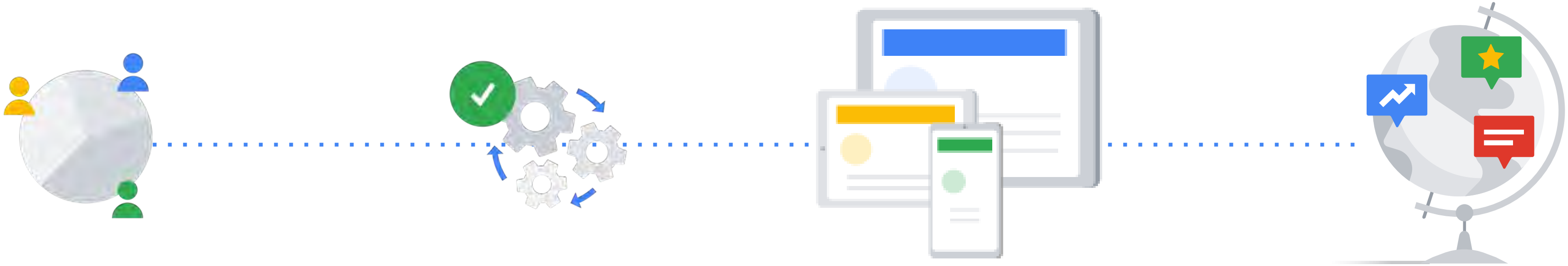
Baby steps

Organizational

Procedural

Product

Global view



Organization

Problem

Shortage of 2M[1] Security Professionals

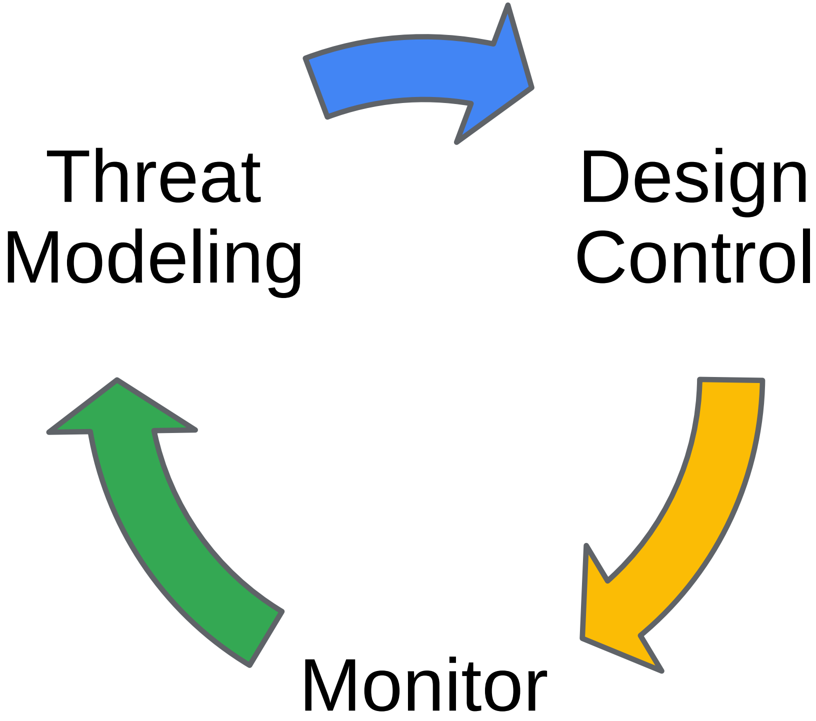
With a small reactive staff, incidents will occur.[2]

Action

Define 5 organizational maturity levels[3]

Develop awareness and processes internally

Process & Product



01

Threat Modeling

Threat modeling

What is it?

- A light-weight, iterative process to simulate attacks on the product
- Key Principle of Security Management & guidance [31, 32]

Why use it?

- Threats vary **greatly** by device, environment and use case
- Highlights potential gaps and mitigations
- Use it to identify probably threat tiers[1]

How?

- Use small focused teams with light documentation
- Iterate in cadence with design reviews
- Output inspires Vulnerability, Asset and Threat library[33]

Threat modeling

Enumerate Assets	Identify Boundaries	STRIDE[1,2]	Address
List the items you are protecting	Create Data Flow Diagram (DFD)	Identify potential threats	Mitigate, Defer , Accept or Eliminate
Reference the intended use and safety risks	Decompose application (SAD)	Reference current trends, standards	Ensure documentation

Key Action

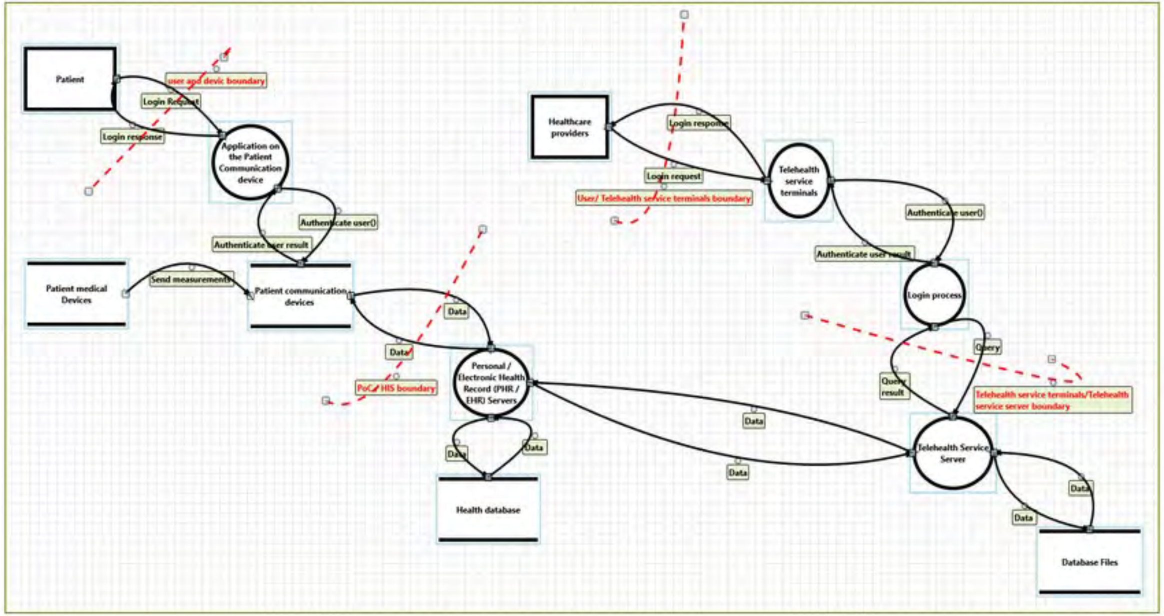
Threat modeling should be fast, repeatable and low friction to identify gaps

Data Flow Diagram (example)

Repeatable exercise

Keep it simple and loose.

Focus on control boundaries



Source: Abomhara, Mohamed & Køien, Geir & Gerdes, Martin. (2015). A STRIDE-Based Threat Model for Telehealth Systems.

Vulnerability

What is it?

- A weakness that can be exploited by a threat

How is it created?

- Conscious Design , Unintended implementation, Unforeseen Development

How is it Mitigated?

- Identified using Threat Models, V&V Testing (e.g: penetration testing) and Monitoring (e.g: NVD, Scans)
- Determine relevance and rank them using using CVSS[34]
- Prefer to use semi-quantitative scales to preserve speed

Key Action

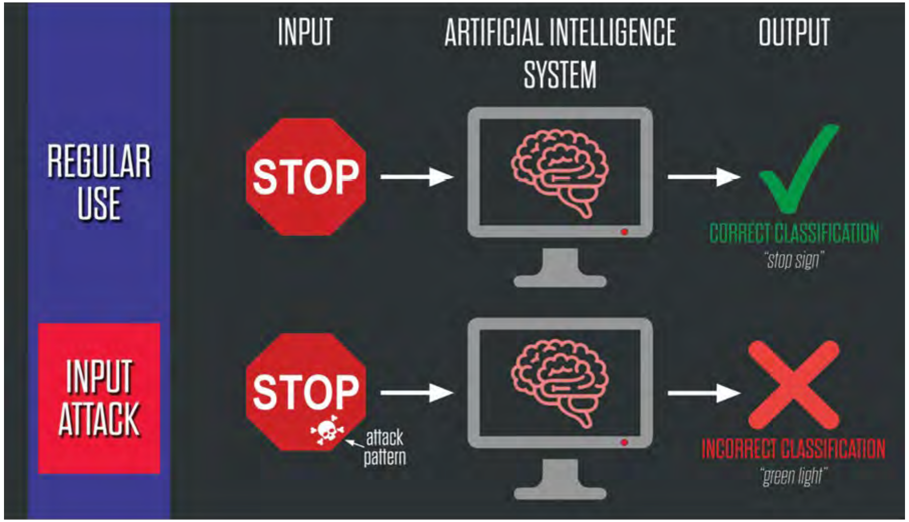
Vulnerabilities across shared OTS systems should be prioritized

Case Study 1: Hospitals and Medical Devices[35]

- Overview of current hospital systems, simulated attacks and mitigations
- Successful remote attempts as well as from the kiosks at the hospital
- Mixed-Asset management was ineffective
- Connected medical devices need to be hardened by default

Source: ISE research Study

Case Study 2: AI and trained models [36,37]



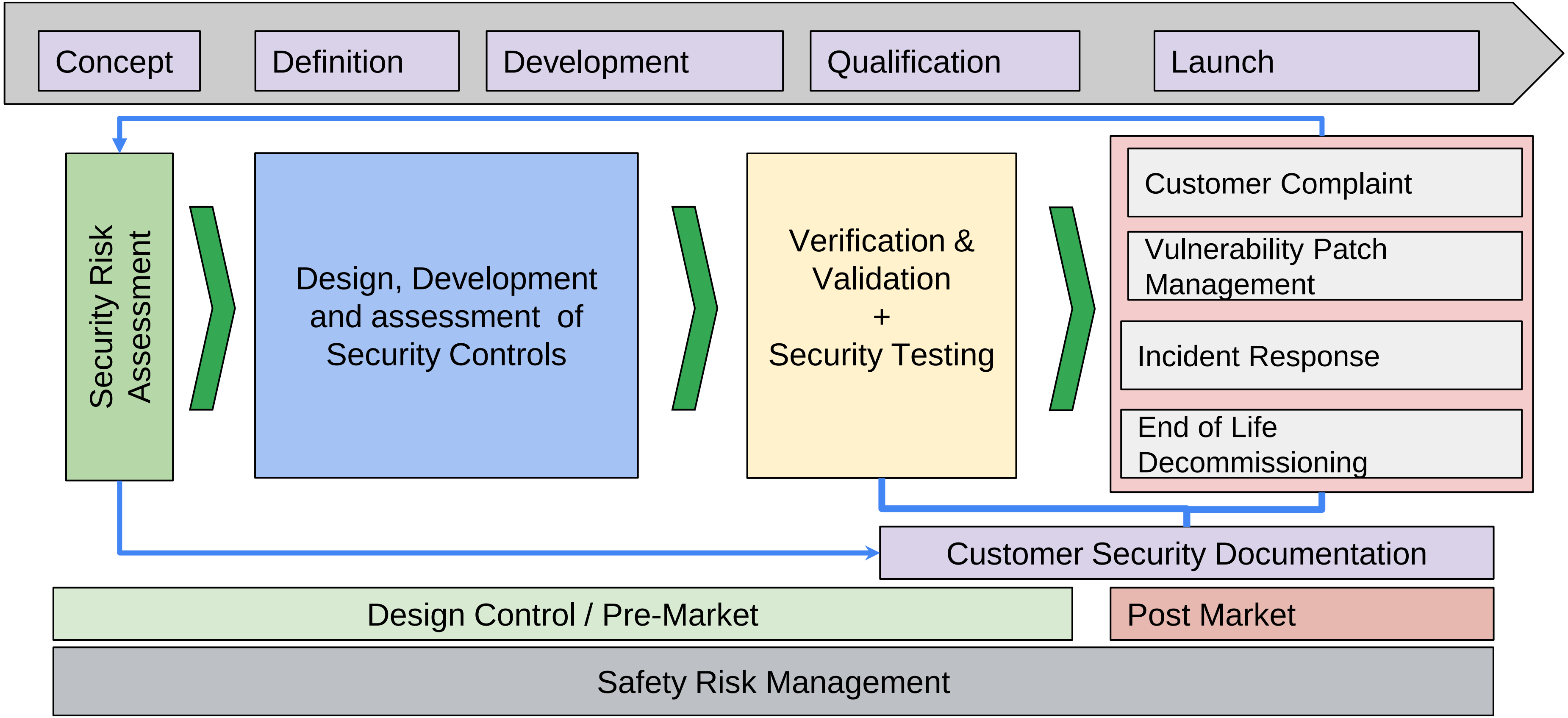
- Overview of potential threats to Artificial Intelligence/ Machine Learning products
- AI/ML-centric threats have different vectors and goals
- "Dataset poisoning" in medical applications (small datasets, high risk)
- AI attacks cannot be patched easily

Harvard paper:
Hackaday Paper explanation

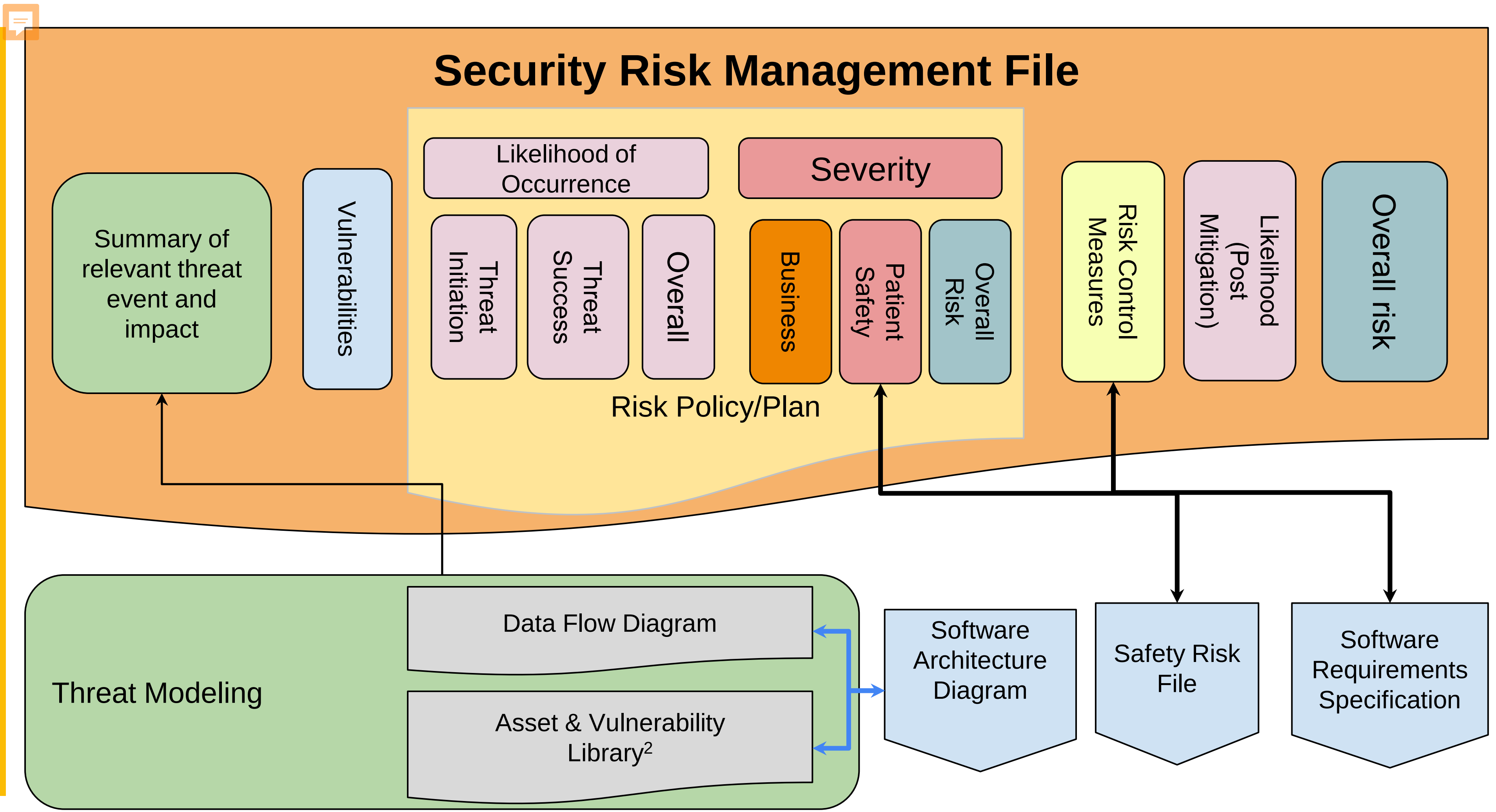
02

Design Control

Procedural view



Source: JSP, minor edits


Security Risk Management File
Summary of relevant threat event and impact
Vulnerabilities
Likelihood of Occurrence
Threat Initiation
Threat Success
Overall
Severity
Business
Patient Safety
Overall Risk
Risk Policy/Plan
Risk Control Measures
Likelihood (Post Mitigation)
Overall risk
Threat Modeling
Data Flow Diagram
Asset & Vulnerability Library2
Software Architecture Diagram
Safety Risk File
Software Requirements Specification

Documentation

Most of the items mentioned above are existent design documents. Keep the final assets as part of the Design History File (DHF)

Submit as required by guidance documents for the pertinent geography (See slides 18-19).

Following the JSP and accepted standards should meet expectations for additional information requests

Key Action

Penetration test and SRMF seem to be consistent request by authorities

03

Monitor

Monitoring

Surveillance

Vulnerability Management

Customer Feedback

Communication

Coordinated Disclosure[38]

Bills of Materials

Operations Manual

Lifecycle

Patch Management

End-of-Life

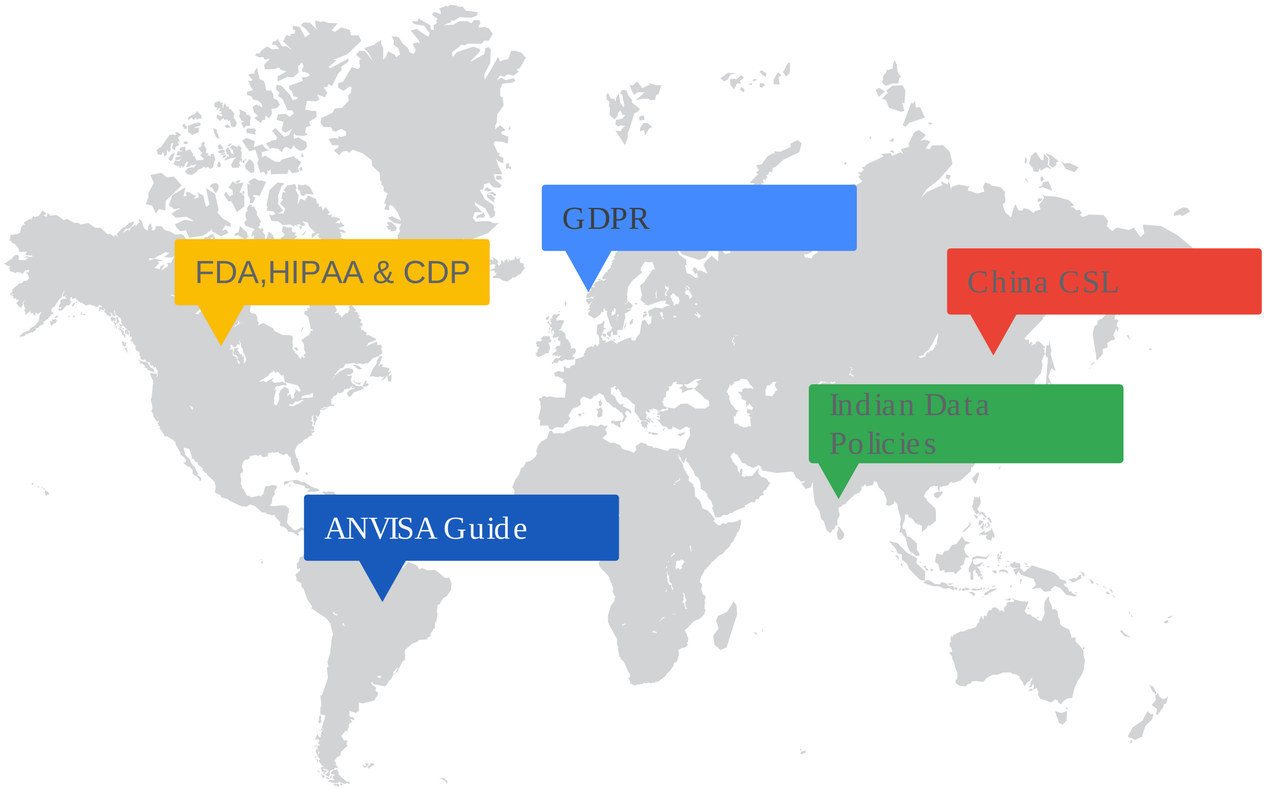
Bill of Materials (💣)

What is it?

- List of third party SW components necessary for functionality.
- Intended to promote transparency and empowerment of HDOs

How do we handle this?

Global view



GDPR
FDA,HIPAA & CDP
China CSL
Indian Data Policies
ANVISA Guide

“If you think you know-it-all about cybersecurity, this discipline was probably ill-explained to you.”

Stephane Nappo

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Thank You

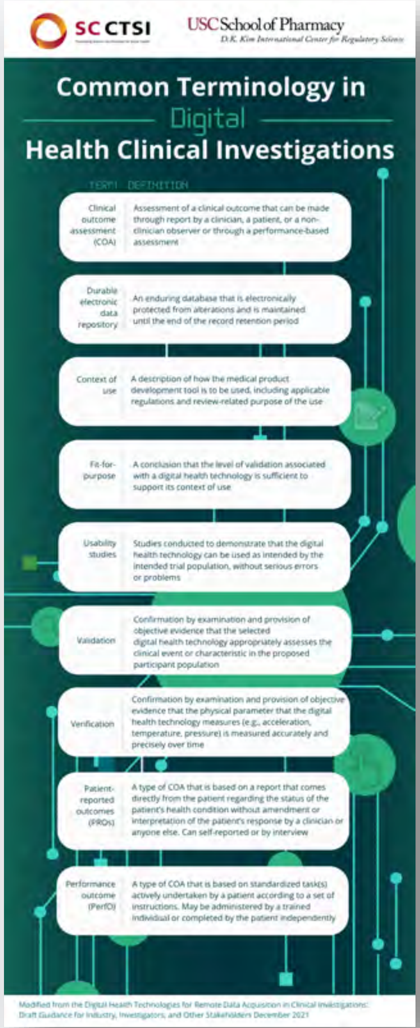
Regulatory Science Symposium

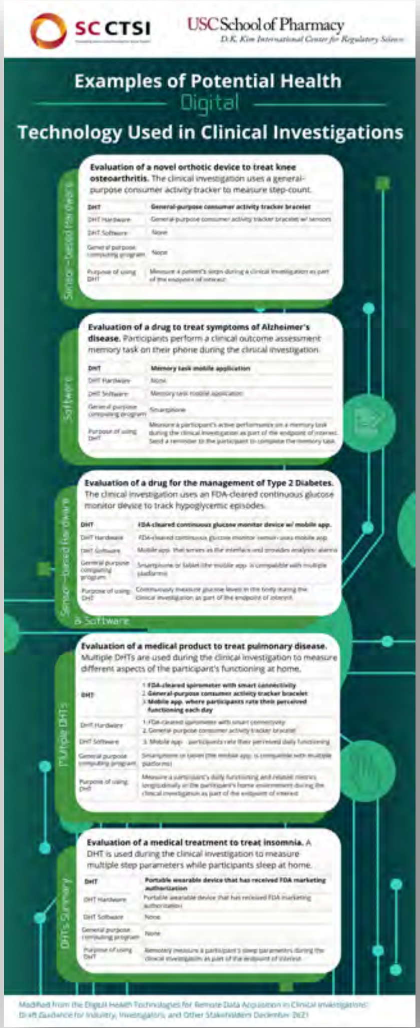
Emerging Technologies in the Medical Device Industry

Wrap-Up!

Susan Bain, DRSc
Assistant Professor, Regulatory and Quality Sciences

Resource





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This certifies that

Before the end of today's symposium, you will receive a link to take the program evaluation.

Follow this link to the Survey:

Take the Survey

Please complete the program evaluation to receive a certificate of completion by Friday, October 7, 2022.

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