Virtual Reality in Stroke Rehabilitation:  
Results from

Efficacy of Virtual Reality Exercises in Stroke Rehabilitation

Gustavo Saposnik, MD, MSc, FAHA, FRCPC  
Associate Professor of Medicine (Neurology)  
Director, Center for Virtual Reality studies (CVR)  
St. Michael's Hospital - University of Toronto  
saposnikg@smh.ca

On behalf of EVREST Investigators for the Stroke Outcomes Research Group (SORCan-www.sorcan.ca)

Leonardo G. Cohen, MD; Muhammad Mamdani, PharmD MPH; Sepideth Pooyania, MD; Michelle Ploughman, MD; Donna Cheung, PT; Jennifer Shaw, RhT; Judith Hall, MSc; Peter Nord, MD; Sean Dukelow, MD; Yongchai Nilanont, MD; Felipe De los Rios La Rosa, MD; Lisandro Olmos, MD; Mindy Levin, PhD; Robert Teasell, MD; Ashley Cohen, MSc; Kevin Thorpe, MMath; Andreas Laupacis, MD; Mark Bayley, MD (Co-PI).

ClinicalTrials.gov # NTC01406912
Dr. Gustavo Saposnik
EVREST Multicenter

FINANCIAL DISCLOSURE:
Dr. Saposnik is supported by the Distinguished Clinician-Scientist Award given by Health and Stroke Foundation of Canada followed an open peer-reviewed competition

UNLABELED/UNAPPROVED USES DISCLOSURE:
Nothing to disclose
Virtual reality (VR) is a computer-based technology that allows users to interact with a multisensory simulated environment and receive ‘real-time’ feedback on performance.

Limited evidence from small, single-center studies suggested modest beneficial effects on stroke recovery.

There has been rapid adoption of virtual reality as a rehabilitation strategy.

However, its effectiveness has not been established.
Objectives

We compared the efficacy of VR with recreational therapy (active control) added to customary care on motor recovery among patients who suffered an acute ischemic stroke.

Hypothesis

VR after stroke results in better motor recovery of the upper extremity required for ADLs relative to recreational activities as add-on therapies to conventional rehabilitation.
Rationale

- **Limitations of conventional rehabilitation** (e.g. modest effect, resource and therapy intensive, poor adherence)

- **Pilot data** (30% improvement in the pilot study- Saposnik et al Stroke 2010; 41:1477-84)

- **Meta-analysis** (Saposnik et al. Stroke 2011; PlosMedicine 2015, Cochrane Review 2015)

- **Application of relevant rehab concepts**
  - Repetitive, task-specific activities
  - ‘Mirror neuron system’ (activation of a set of neurons when individuals observe an action being performed by someone else)
  - Enhancing brain reward system (Motivation)
All participants received customary rehabilitation as standard of care at each institution.

**Design**

Efficacy of Virtual Reality Exercises in STroke Rehabilitation

Eligible patients
Chedocke McMaster >3 (arm/hand) ≤ 3 months

n = 140

Randomized
Single blinded, trial
Two parallel groups

Recreational Therapy (RT) *
n = 70

Virtual Reality Wii (VR Wii) *
n = 70

10 sessions within 14 days, 60 min each

**Primary end points:** Efficacy- Wolf MFT
Secondary end-points: Box & Block Tests, QoL, FIM, Grip, RPS

Assessments
Baseline End of intervention 4-weeks post-intervention
Inclusion & exclusion Criteria

**Inclusion**
- Written informed consent prior to entry into the study AND
- In-patient at the time of randomization AND
- Aged over 18 and younger than 85 AND
- Evidence of ischemic stroke confirmed by CT or MRI head AND
- Onset of symptoms within 3 months prior to randomization AND
- Measurable Chedoke-McMaster scale > 3 in the affected arm or hand AND
- Functional independence prior to present stroke (baseline mRS = 0-1) AND
- Patient is alert, medically stable according to the treating physician and able to follow simple verbal commands

**Exclusion**
- Acute stroke onset more than 3 months ago
- Patient is unable to follow verbal commands (global aphasia)
- Severe illness with life expectancy less than 3 months (cancer, endocarditis, metastasis with an occult primary malignancy, coagulopathy).
- Uncontrolled hypertension according to the treating physician
- Pain or joint problems limiting movement of the arm (e.g. shoulder pain)
- Unstable angina, recent myocardial infarction or CHF
- Any history of seizure, except for febrile seizures of childhood
- Participation in another clinical trial involving rehabilitation.
- Any medical condition that might confound the interpretation of results or put the patient at risk (amputation of one extremity).
**Intervention (Wii protocol)**

- Focus on the upper extremity
- 10 Wii sessions within 2-weeks
- 60 min. each
- Sitting position
- Supervised sessions

- Participants were instructed to use the affected arm/hand
- May use a velcro strap
- Games: 30’ Wii Sports® and Game Party 3®)
- Setting: lights ON, 6 feet away from the TV
Active control (Recreational therapy)

- Similar format & schedule as Wii protocol

- Patients were be instructed to use the affected arm/hand.

- Recreational activities:
  - Matching cards
  - Domino
  - Ball game
  - ‘Jenga’

- Sitting position
- Supervised sessions
**Results**

- **893 Individuals Screened**
  - 752 Not Eligible
    - Age criteria: 106
    - Too mild or severe deficit: 282
    - Medical reasons: 240
    - Others: 124
  - 47 Refused Consent
- **141 Randomized**
  - 71 Assigned to Receive Wii Virtual Reality Therapy
    - 4 Participants who discontinued after training session
    - 13 Participants discontinued prior to completion of 10 sessions
    - 5 Participants completed post-intervention
    - 59 completed post-intervention
    - 47 completed the 4-week post intervention assessment
    - 59 included in the primary analysis
  - 70 Assigned to Receive Recreational Therapy
    - 0 Participants who discontinued after training session
    - 57 Participants who completed all 10 sessions
    - 54 completed post-intervention
    - 54 completed the 4-week post intervention assessment
    - 62 included in the primary analysis

**Discussion**

**Conclusions**

- 15.8%
- 83.1%
- 88.6%
## Results

<table>
<thead>
<tr>
<th>Characteristics*</th>
<th>Combined (n=141)</th>
<th>RT (n=70)</th>
<th>VRWii (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age</strong> (range), years</td>
<td>63 (55, 70)</td>
<td>62 (57, 71)</td>
<td>64 (54, 69.5)</td>
</tr>
<tr>
<td><strong>Sex</strong>, male</td>
<td>94 (67)</td>
<td>48 (69)</td>
<td>46 (65)</td>
</tr>
<tr>
<td><strong>Stroke severity, CNS median (IQR)</strong></td>
<td>8.5 (7.5, 9.5)</td>
<td>8.5 (7.5, 9.0)</td>
<td>8.5 (7.5, 9.9)</td>
</tr>
<tr>
<td><strong>Stroke subtype</strong>, Lacunar</td>
<td>62 (47%)</td>
<td>31 (46)</td>
<td>31 (48)</td>
</tr>
<tr>
<td>Non-Lacunar</td>
<td>69 (53%)</td>
<td>36 (54)</td>
<td>33 (52)</td>
</tr>
<tr>
<td><strong>Affected side</strong>, Left</td>
<td>75 (53%)</td>
<td>39 (56)</td>
<td>36 (51)</td>
</tr>
<tr>
<td><strong>Chedoke-McMaster, median [IQR]</strong></td>
<td>5 (4, 5)</td>
<td>5 (4, 5)</td>
<td>4 (3, 5)</td>
</tr>
<tr>
<td><strong>Modified Rankin Scale</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>60 (43%)</td>
<td>27 (39%)</td>
<td>33 (46%)</td>
</tr>
<tr>
<td>3-5</td>
<td>81 (57%)</td>
<td>43 (61%)</td>
<td>38 (54%)</td>
</tr>
<tr>
<td><strong>Days from onset to randomization</strong> (median, IQR)</td>
<td>25 (9, 46)</td>
<td>24.5 (10, 41)</td>
<td>27.0 (9.0, 53)</td>
</tr>
<tr>
<td><strong>Time (min) of conventional rehabilitation</strong>, Median (IQR)</td>
<td>340 (105, 545)</td>
<td>358 (120, 555)</td>
<td>330 (95, 543)</td>
</tr>
<tr>
<td><strong>Time (min) of duration of intervention</strong>, median (IQR)</td>
<td>600 (560, 600)</td>
<td>600 (573, 600)</td>
<td>595 (550, 600)</td>
</tr>
<tr>
<td>% of delivered from scheduled interventions</td>
<td>89.1%</td>
<td>90.2%</td>
<td>88.0%</td>
</tr>
</tbody>
</table>

Numbers between brackets represent %, unless otherwise indicated.
Results – Primary Outcome

Median changes in WMFT

% improvement in WMFT from baseline

Lower is better

VRWii

RT

p-value: 0.47
Results – Secondary Outcomes

**Grip strengths (in Kg)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End of intervention</th>
<th>4-weeks post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RT</strong></td>
<td>15.4</td>
<td>17.9</td>
<td>17.8</td>
</tr>
<tr>
<td><strong>VRWii</strong></td>
<td>11.5</td>
<td>14.8</td>
<td>15.9</td>
</tr>
</tbody>
</table>

Higher is better

**p-value: 0.71**

**Stroke Impact Scale (hand function)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End of intervention</th>
<th>4-weeks post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RT</strong></td>
<td>13.2</td>
<td>18.0</td>
<td>20.4</td>
</tr>
<tr>
<td><strong>VRWii</strong></td>
<td>13.0</td>
<td>17.0</td>
<td>18.5</td>
</tr>
</tbody>
</table>

Higher is better

**p-value: 0.31**
Results – Quality of the movement

Reaching Performance Scale (RPS)

**Close Target** (6 tasks)
- Baseline: 13.9
- End of intervention: 15.9
- 4-weeks post-intervention: 15.4

**Far Target** (6 tasks)
- Baseline: 14.2
- End of intervention: 15.5
- 4-weeks post-intervention: 14.7

Higher is better.

p-value: 0.83

p-value: 0.81
### Efficacy Outcomes

#### Primary Outcome Measure

<table>
<thead>
<tr>
<th>RT (n=70)</th>
<th>VRWii (n=71)</th>
<th>Between Group Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td><strong>Follow-Up</strong></td>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td>WMFT at the end of the intervention, mean (SD) total time in seconds</td>
<td>68.41 (101.24)</td>
<td>39.81 (35.45)</td>
</tr>
<tr>
<td>WMFT at the end of the intervention, median (IQR) total time in seconds</td>
<td>38.0 (28.0-64.1)</td>
<td>23.0 (17.4-36.6)</td>
</tr>
</tbody>
</table>

#### Secondary Outcome Measures

| WMFT 4-weeks post intervention, mean (SD) total time in seconds | 68.41 (101.24) | 50.59 (120.71) | 91.9 (122.25) | 45.5 (51.29) | **-14.17 (-52.02, 23.68)** | **0.3463** |
| WMFT 4-weeks post intervention, median (IQR) total time in seconds | 38.0 (28.0-64.1) | 27.1 (21.2-45.5) | 43.7 (26.1-68.0) | 29.7 (21.4-45.2) | **-2.6 (-2.8, 9.27)** | **0.2948** |

| BBT: mean number of blocks | 24.2 (14.15) | 30.85 (13.17) | 22.93 (14.37) | 30.45 (17.66) | **-3.43 (-6.13, -0.74)** | **0.0177** |
| Barthel index, mean | 64.23 (22.97) | 80.29 (21.72) | 64.69 (22.37) | 83.44 (17.99) | **3.5 (-2.28, 9.27)** | **0.2948** |
| 4-weeks post-intervention | 64.23 (22.97) | 89.33 (16) | 64.69 (22.37) | 90.21 (13.76) | **0.83 (-4.34, 6)** | **0.7735** |

| Functional independence measure (FIM), mean | 92.59 (19.88) | 106.11 (17.61) | 95.7 (18.96) | 108.8 (16.16) | **0.88 (-3.41, 5.18)** | **0.7352** |
| 4-weeks post-intervention | 92.59 (19.88) | 111.69 (15.11) | 95.7 (18.96) | 113.62 (13.05) | **0.78 (-3.94, 5.49)** | **0.8477** |

| SIS hand function | 13.21 (5.6) | 18 (6.09) | 13.02 (6.36) | 16.98 (6.52) | **-1.07 (-2.88, 0.74)** | **0.314** |

| 4-weeks post-intervention | 13.21 (5.6) | 20.37 (5.25) | 13.02 (6.36) | 18.5 (5.97) | **-2.08 (-4.15, -0.01)** | **0.0743** |

| SIS S16 | 83.14 (22.62) | 101.63 (23.42) | 88.65 (25.54) | 104.02 (21.62) | **-2.2 (-8.52, 4.13)** | **0.4935** |
| 4-weeks post-intervention | 83.14 (22.62) | 112.65 (21.33) | 88.65 (25.54) | 112.79 (20) | **-2.84 (-10.16, 4.49)** | **0.5137** |

| SIS perception of recovery | 52.79 (18.64) | 67.13 (16.49) | 58.33 (22.82) | 66.04 (21.26) | **-4.36 (-10.87, 2.16)** | **0.2522** |

| 4-weeks post-intervention | 52.79 (18.64) | 71.62 (15.49) | 58.33 (22.82) | 70.52 (19.16) | **-2.27 (-8.54, 4.01)** | **0.3521** |

| Grip strength: mean in kg | 15.35 (9.41) | 17.88 (9.75) | 11.5 (9.79) | 14.8 (10.29) | **0.23 (-1.8, 2.27)** | **0.7127** |

| 4-weeks post-intervention | 15.35 (9.41) | 17.83 (9.64) | 11.5 (9.79) | 15.89 (10.14) | **-1.17 (-3.17, 0.83)** | **0.3583** |

† Adjusted by age, sex, treatment arm, baseline Chedoke score, stroke severity, and baseline measure as appropriate
### Adverse events

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>RT n = 70 (%)</th>
<th>VRWii n = 71 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>12 (17)</td>
<td>10 (15)</td>
</tr>
<tr>
<td>Lightheadness</td>
<td>8 (11)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (6)</td>
<td>4 (6)</td>
</tr>
<tr>
<td>Pins and needless</td>
<td>10 (14)</td>
<td>10 (15)</td>
</tr>
<tr>
<td>Numbness</td>
<td>33 (47)</td>
<td>19 (28)</td>
</tr>
<tr>
<td>Muscle aches</td>
<td>29 (41)</td>
<td>18 (27)</td>
</tr>
<tr>
<td>Back pain</td>
<td>33 (47)</td>
<td>30 (45)</td>
</tr>
<tr>
<td>Fatigue (post-intervention)</td>
<td>44 (63)</td>
<td>38 (57)</td>
</tr>
<tr>
<td>Headache</td>
<td>13 (19)</td>
<td>9 (13)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (14)</td>
<td>10 (15)</td>
</tr>
<tr>
<td><strong>Serious adverse events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (1.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>0 (0)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Seizures</td>
<td>1 (1.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>All</strong></td>
<td>2 (3.2)</td>
<td>1 (1.7)</td>
</tr>
</tbody>
</table>
Subgroup analysis

Adjusted Estimates (95%CI)

- Favors RT
  - >=63 Years Old: 1.18 (-1.54, 3.89)
  - <63 Years Old: -1.18 (-3.89, 1.54)
  - Male: 1.14 (-1.84, 4.12)
  - Female: -1.14 (-4.12, 1.84)
  - Right-Handed: -1.38 (-7.48, 4.71)
  - Left-Handed: 1.38 (-4.71, 7.48)
  - CNS Score >= 8.5: -2.13 (-5.09, 0.84)
  - CNS Score < 8.5: 2.13 (-0.84, 5.09)
  - Chedoke Score >=5: 0.1 (-2.83, 3.02)
  - Chedoke Score <5: -0.1 (-3.02, 2.83)
  - Stroke to Randomization > 10 Days: 2.25 (-1.07, 5.58)
  - Stroke to Randomization <= 10 Days: -2.25 (-5.58, 1.07)
  - FIM >= 97: 0.44 (-2.47, 3.35)
  - FIM <97: -0.44 (-3.35, 2.47)

- Favors VRWii
  - >=63 Years Old: 1.18 (-1.54, 3.89)
  - <63 Years Old: -1.18 (-3.89, 1.54)
  - Male: 1.14 (-1.84, 4.12)
  - Female: -1.14 (-4.12, 1.84)
  - Right-Handed: -1.38 (-7.48, 4.71)
  - Left-Handed: 1.38 (-4.71, 7.48)
  - CNS Score >= 8.5: -2.13 (-5.09, 0.84)
  - CNS Score < 8.5: 2.13 (-0.84, 5.09)
  - Chedoke Score >=5: 0.1 (-2.83, 3.02)
  - Chedoke Score <5: -0.1 (-3.02, 2.83)
  - Stroke to Randomization > 10 Days: 2.25 (-1.07, 5.58)
  - Stroke to Randomization <= 10 Days: -2.25 (-5.58, 1.07)
  - FIM >= 97: 0.44 (-2.47, 3.35)
  - FIM <97: -0.44 (-3.35, 2.47)
Our study only informs about non-immersive VR technology (chosen as it is low cost, less complex and easier to deliver relative to immersive VR systems).

Relatively short duration of our add-on intervention.
Nevertheless, it is similar to other VR interventions as summarized in three meta-analysis from previous positive studies.

Lack of an additional arm receiving conventional therapy alone.
However, this approach has been criticized by artificially creating potential benefits to the VR technology arm when those participants actually received longer therapy.

No information on bimanual tasks.
Participants randomized to either VR or RT groups had a similar improvement.

There was no additional benefit of VR relative to RT.

Our results support the concept that the type of task may be less relevant, as long as, it is intensive enough and task-specific. This concept is supported by previous studies applying innovative technologies (e.g. arm robotics) with active control groups showing the intervention is beneficial but not better than active controls (Lo et al. NEJM 2010; 362: 1772-83; Duncan et al. NEJM 2011; 364:2026-36)

Low- and middle-income countries (constraint of resources, limited access to technologies, and time spent in rehabilitation):
  - Simple, low-cost, high-intensity and effective task-specific home-based therapies (e.g. RT) would contribute to optimize motor recovery.
Conclusions

Among participants who suffered a stroke in the previous 2 months with a mild-moderate motor impairment,

- VR as an add-on therapy to conventional rehabilitation was not superior to intensive recreational therapy in improving motor function, grip strength, hand function, quality of movement, or quality of life.

- Our findings caution against the wide use and routine implementation of non-immersive VR technology as add-on strategies (over RT) in neuro-rehabilitation after stroke.
Acknowledgements

- **To all participants**
- **Co-Investigators**
  - Site PI’s and team
  - Dr. Muhammad Mamdani (AHRC)
  - Dr. Mark Bayley (TRI)
  - Donna Cheung (SMH)
  - Jennifer Shaw (TRI)
  - Dr. Bob Teasell
  - Dr. Leonardo Cohen (NINDS-NIH)
  - Dr. Andreas Laupacis (LKS)

- **Li Ka Shing Institute at St. Michael’s Hospital**
  - Kevin Thorpe
  - Judith Hall
  - Ashley Cohen

- **To our sponsors**

- **Supporting Institutions**
  - Li Ka Shing Institute
Thank You  
Mahalo 
Kiitos 
Toda 
Gracias 
Obrigado 
Takk 
Grazie 
Thanks 
Merci
Results

Cumulative recruitment

- Actual Recruitment
- Linear (Anticipated Recruitment)

Number of participants randomized

- 2012
- 2013
- 2014
- 2015
Masking

Blind assessor was correct

- Guessed: 55%
- Expected: 50%

p-value = 0.24