Traumatic Brain Injury and Hyperbaric Oxygen Therapy Dawn of a New Day

E Geroge Wolf

59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
JBSA-Lackland, TX 78236-9908
210-292-7141

Approved for public release. Distribution is unlimited.

19a. NAME OF RESPONSIBLE PERSON
Clarice Longoria

19b. TELEPHONE NUMBER (include area code)
210-292-7141
Traumatic Brain Injury and Hyperbaric Oxygen Therapy: Dawn of a New Day
APWCA 16th Annual National Clinical Conference
7-9 Sep 17

Dr. E. George Wolf (study director)
Hyperbaric Medicine
San Antonio, TX
210-359-8018
earl.g.wolf.ctr@mail.mil
Disclaimer

• The opinions expressed in this document are solely those of the author and do not represent an endorsement by or the views of the United States Air Force, the Department of Defense, or the United States Government.
Disclaimer

- The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402
Statistics

• 1.4 million TBIs occur annually in the US
• Mild traumatic brain injury: incidence of 180/100,000 population
• Department of Defense: 361,092 TBIs for period Jan 2000 through Dec 2015 with 297,478 mild TBI

AHRQ Comments

- Agency for Healthcare Research and Quality:
  - the uncertainty about the frequency and severity of serious adverse events underlies much of the controversy about HBOT
  - the case against HBOT is based on the reasoning that, because HBOT may be harmful, it must be held to the highest standard of proof
  - if HBOT can be shown to be as safe as its supporters believe it to be, the standard of proof of its efficacy can be lowered

Materials and Methods

- Exposures include sham (1.3 ATA air) and treatment profile (2.4 ATA 100% oxygen) – 25/group
- Each group to have 30 exposures
- History and physical done prior to exposures
  - Focused on concussion history and baseline symptoms
- Composite scores obtained prior to intervention, after every 5 exposures and at 6 week follow-up
  - ImPACT
  - Braincheckers (ANAM)
  - PCL-M
Results 1st Publication

- Hyperbaric side effects: no statistical difference between groups with ear and sinus blocks most predominate
  - Included traditional side effects as well as any medical issue that occurred during the study.
  
AHRQ Comments

• Agency for Healthcare Research and Quality:
  • If there is a 1 percent chance that the treatment works, a rational decision maker would try it—there is a potential gain and no potential loss.
  • On the other hand, if there are proven harms, and their severity and frequency are well described, the probability that the treatment works would have to be higher before most people would try it

Materials and Methods

• Repeated measures analysis of covariance (ANCOVA)
• Repeated measures analysis of variance (RMANOVA)
  • Both used to test for differences between groups
  • No significant statistical difference between groups, but both groups improved
• Relative risk of improvement – ad hoc
  • MedCalc (http://www.medcalc.org)
  • Used to analyze responders versus non-responders between each exposure group for each composite score
  • Calculated for concussion history categories
Materials and Methods

• ImPACT: verbal memory, visual memory, processing speed and response time
• Braincheckers (ANAM): code substitution, procedural reaction time, Go-NoGo reaction time, matching to sample, code substitution recall, and simple reaction time
  • Composite score for both speed and accuracy
• PCL-M: composite scores only
• Concussion history: # of concussive events, multiple non-concussive events, two concussive events within 48 hours, time expired from the last concussion to consent, etiology of concussion, and loss of consciousness.
Concussion Symptoms

Somatic Symptoms
- Headaches
- Visual Problems
- Dizziness
- Noise/Light Sensitivity
- Nausea

Emotionality
- More emotional
- Sadness
- Nervousness
- Irritability

Cognitive Symptoms
- Attention Problems
- Memory dysfunction
- “Fogginess”
- Fatigue
- Cognitive slowing

Sleep Disturbance
- Difficulty falling asleep
- Sleeping less than usual

- More emotional
- Sadness
- Nervousness
- Irritability
<table>
<thead>
<tr>
<th>Number</th>
<th>Consent</th>
<th>Event Delay</th>
<th>Event</th>
<th>Ex To Con</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>7127</td>
<td>May 10</td>
<td>0</td>
<td>0</td>
<td>Apr 08</td>
<td>25</td>
</tr>
<tr>
<td>7258</td>
<td>Mar 10</td>
<td>1</td>
<td>0</td>
<td>Jul 07</td>
<td>32</td>
</tr>
<tr>
<td>7356</td>
<td>Oct 06</td>
<td>1</td>
<td>0</td>
<td>Mar 05</td>
<td>43</td>
</tr>
<tr>
<td>7303</td>
<td>Jan 10</td>
<td>0</td>
<td>0</td>
<td>Mar 05</td>
<td>58</td>
</tr>
<tr>
<td>7409</td>
<td>Mar 10</td>
<td>1</td>
<td>0</td>
<td>Mar 08</td>
<td>24</td>
</tr>
<tr>
<td>7526</td>
<td>Jul 09</td>
<td>0</td>
<td>0</td>
<td>Nov 08</td>
<td>8</td>
</tr>
<tr>
<td>7650</td>
<td>Jul 07</td>
<td>0</td>
<td>0</td>
<td>Feb 07</td>
<td>5</td>
</tr>
<tr>
<td>7756</td>
<td>Mar 10</td>
<td>1</td>
<td>1</td>
<td>Jul 08</td>
<td>8</td>
</tr>
<tr>
<td>7811</td>
<td>Oct 09</td>
<td>0</td>
<td>0</td>
<td>Apr 07</td>
<td>30</td>
</tr>
<tr>
<td>7927</td>
<td>Oct 09</td>
<td>1</td>
<td>0</td>
<td>Jun 07</td>
<td>28</td>
</tr>
<tr>
<td>7642</td>
<td>May 10</td>
<td>1</td>
<td>0</td>
<td>Dec 08</td>
<td>18</td>
</tr>
<tr>
<td>7717</td>
<td>Aug 10</td>
<td>1</td>
<td>0</td>
<td>Jan 06</td>
<td>55</td>
</tr>
<tr>
<td>7954</td>
<td>Jul 30</td>
<td>1</td>
<td>0</td>
<td>Apr 06</td>
<td>51</td>
</tr>
<tr>
<td>7991</td>
<td>Feb 09</td>
<td>1</td>
<td>0</td>
<td>Mar 07</td>
<td>25</td>
</tr>
<tr>
<td>7727</td>
<td>Apr 09</td>
<td>1</td>
<td>1</td>
<td>Nov 07</td>
<td>18</td>
</tr>
<tr>
<td>7941</td>
<td>Sep 30</td>
<td>1</td>
<td>0</td>
<td>Nov 04</td>
<td>70</td>
</tr>
<tr>
<td>7756</td>
<td>Mar 09</td>
<td>1</td>
<td>0</td>
<td>Aug 07</td>
<td>18</td>
</tr>
<tr>
<td>7856</td>
<td>Sep 09</td>
<td>1</td>
<td>0</td>
<td>Apr 06</td>
<td>58</td>
</tr>
<tr>
<td>7941</td>
<td>Apr 09</td>
<td>1</td>
<td>0</td>
<td>Sep 06</td>
<td>29</td>
</tr>
<tr>
<td>7941</td>
<td>Nov 09</td>
<td>0</td>
<td>0</td>
<td>Dec 03</td>
<td>71</td>
</tr>
<tr>
<td>7972</td>
<td>Aug 30</td>
<td>0</td>
<td>0</td>
<td>Jul 06</td>
<td>48</td>
</tr>
<tr>
<td>7628</td>
<td>Jun 06</td>
<td>1</td>
<td>0</td>
<td>Jun 09</td>
<td>12</td>
</tr>
<tr>
<td>7821</td>
<td>Sep 09</td>
<td>0</td>
<td>0</td>
<td>Oct 06</td>
<td>35</td>
</tr>
<tr>
<td>7837</td>
<td>Jan 10</td>
<td>1</td>
<td>0</td>
<td>Feb 08</td>
<td>47</td>
</tr>
<tr>
<td>7450</td>
<td>Jul 10</td>
<td>1</td>
<td>0</td>
<td>Apr 06</td>
<td>51</td>
</tr>
<tr>
<td>7370</td>
<td>Oct 09</td>
<td>1</td>
<td>0</td>
<td>Oct 08</td>
<td>9</td>
</tr>
<tr>
<td>7757</td>
<td>Oct 09</td>
<td>1</td>
<td>0</td>
<td>Aug 07</td>
<td>76</td>
</tr>
<tr>
<td>7817</td>
<td>Mar 09</td>
<td>0</td>
<td>0</td>
<td>Jun 07</td>
<td>21</td>
</tr>
<tr>
<td>7718</td>
<td>May 09</td>
<td>1</td>
<td>1</td>
<td>Jul 07</td>
<td>22</td>
</tr>
<tr>
<td>7828</td>
<td>Sep 10</td>
<td>1</td>
<td>0</td>
<td>Nov 05</td>
<td>58</td>
</tr>
<tr>
<td>7416</td>
<td>Mar 10</td>
<td>1</td>
<td>1</td>
<td>Mar 08</td>
<td>22</td>
</tr>
<tr>
<td>7443</td>
<td>Sep 09</td>
<td>0</td>
<td>0</td>
<td>Mar 08</td>
<td>18</td>
</tr>
<tr>
<td>7658</td>
<td>Apr 10</td>
<td>1</td>
<td>1</td>
<td>Sep 06</td>
<td>43</td>
</tr>
<tr>
<td>7858</td>
<td>Apr 09</td>
<td>1</td>
<td>0</td>
<td>Dec 07</td>
<td>76</td>
</tr>
<tr>
<td>7180</td>
<td>Jan 09</td>
<td>1</td>
<td>0</td>
<td>Jul 09</td>
<td>42</td>
</tr>
<tr>
<td>7200</td>
<td>Nov 09</td>
<td>0</td>
<td>3</td>
<td>Feb 07</td>
<td>34</td>
</tr>
<tr>
<td>7328</td>
<td>Jan 09</td>
<td>0</td>
<td>0</td>
<td>Apr 04</td>
<td>62</td>
</tr>
<tr>
<td>7391</td>
<td>Feb 10</td>
<td>1</td>
<td>0</td>
<td>Oct 09</td>
<td>4</td>
</tr>
<tr>
<td>7433</td>
<td>Mar 09</td>
<td>1</td>
<td>0</td>
<td>Jun 06</td>
<td>33</td>
</tr>
<tr>
<td>7727</td>
<td>Sep 10</td>
<td>0</td>
<td>0</td>
<td>Apr 06</td>
<td>53</td>
</tr>
<tr>
<td>7895</td>
<td>Aug 10</td>
<td>0</td>
<td>0</td>
<td>May 10</td>
<td>3</td>
</tr>
<tr>
<td>7900</td>
<td>May 10</td>
<td>1</td>
<td>0</td>
<td>Feb 06</td>
<td>39</td>
</tr>
<tr>
<td>7716</td>
<td>Aug 10</td>
<td>0</td>
<td>0</td>
<td>Aug 09</td>
<td>12</td>
</tr>
<tr>
<td>7538</td>
<td>Jun 10</td>
<td>0</td>
<td>0</td>
<td>Dec 08</td>
<td>39</td>
</tr>
<tr>
<td>7297</td>
<td>Jun 10</td>
<td>0</td>
<td>0</td>
<td>Jan 03</td>
<td>17</td>
</tr>
<tr>
<td>7322</td>
<td>Oct 09</td>
<td>0</td>
<td>1</td>
<td>May 09</td>
<td>5</td>
</tr>
<tr>
<td>7657</td>
<td>May 10</td>
<td>0</td>
<td>0</td>
<td>Aug 07</td>
<td>33</td>
</tr>
<tr>
<td>7856</td>
<td>Oct 09</td>
<td>0</td>
<td>0</td>
<td>May 06</td>
<td>41</td>
</tr>
</tbody>
</table>

Sham improved

ImPACT processing: example of segregated scores

Sham not improved

Withdraw

Treatment not improved

Treatment improved
Results: ImPACT

- # Events
  - 1
  - 2
  - 3
  - 4

- Exposures
  - Multiple
  - Single

- Close event
  - Yes
  - No

- Time to Consent
  - Single event
    - < 1 year
    - < 2 years
    - 2-4 years
    - > 4 years
  - Most recent
    - < 1 year
    - < 2 years
    - 2-4 years
    - > 4 years

- Etiology
  - Blast only
  - Impact only
  - Both

- All Blast
  - All Impact
  - LOC
  - Yes
  - No

- Total
  - Total
  - 2
  - 2
  - 10
  - 4
  - 14
  - 5
  - 6
  - 2

- RMD:
  - 1.5 to 1.49
  - RMD > 1.5
  - RMD > 50% col or row
Results: ImPACT

- All subjects had significant cognitive problems compared with military population
- ANCOVA:
  - no significant differences between groups at any time point for visual memory, verbal memory or reaction time
  - sham was only marginally higher at 30 exposures than the treatment group
- RMANOVA:
  - visual memory and processing time in both groups indicated improvement in each measurement over time
Results – Brainchecker (speed)

<table>
<thead>
<tr>
<th># Events</th>
<th>Code Sub</th>
<th>Procedural RT</th>
<th>Braincheckers Reaction Time (Speed)</th>
<th>Code Sub Recall</th>
<th>Simple Reaction</th>
<th>1.0 to 1.4</th>
<th>&gt; 1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Event Time</th>
<th>Code Sub</th>
<th>Procedural RT</th>
<th>Braincheckers Reaction Time (Speed)</th>
<th>Code Sub Recall</th>
<th>Simple Reaction</th>
<th>1.0 to 1.4</th>
<th>&gt; 1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 4 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most recent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Job Type</th>
<th>Code Sub</th>
<th>Procedural RT</th>
<th>Braincheckers Reaction Time (Speed)</th>
<th>Code Sub Recall</th>
<th>Simple Reaction</th>
<th>1.0 to 1.4</th>
<th>&gt; 1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blunt only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impact only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Blunt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Impact</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total</th>
<th>Code Sub</th>
<th>Procedural RT</th>
<th>Braincheckers Reaction Time (Speed)</th>
<th>Code Sub Recall</th>
<th>Simple Reaction</th>
<th>1.0 to 1.4</th>
<th>&gt; 1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Results – Brainchecker (accuracy)
Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial – UHM 42 (4) 2015
E. George Wolf, Laura M. Baugh, Christine M. Schubert Kabban, Michael F. Richards, Jennifer Prye

- Individual test scores
  - ImPACT:
    - visual memory and processing speed
  - Braincheckers:
    - speed scores in procedural reaction time and simple reaction time
    - accuracy scores for Go-NoGo and simple reaction time
Results: Braincheckers

- **ANCOVA:**
  - scores were not significantly different for any measure between sham and treatment groups

- **RMANOVA:**
  - speed and accuracy scores for code substitution recall, matching to sample, and simple reaction indicated improvement in each measurement over time for both groups
## Results – PCL-M

<table>
<thead>
<tr>
<th># Concussions</th>
<th>Reliable Change</th>
<th>Significant Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposures</th>
<th>Multiple</th>
<th>Single</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Close event</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consent Time</th>
<th>Single event</th>
<th>&lt; 1 year</th>
<th>&lt; 2 years</th>
<th>2-4 years</th>
<th>&gt; 4 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Most recent</th>
<th>&lt; 1 year</th>
<th>&lt; 2 years</th>
<th>2-4 years</th>
<th>&gt; 4 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Blast only</th>
<th>Impact only</th>
<th>Both</th>
<th>All Blast</th>
<th>All Impact</th>
<th>LOC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LOC</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

**Total**: 8

<table>
<thead>
<tr>
<th>RROI: 1.0 to 1.49</th>
<th>RROI &gt; 1.5</th>
<th>RROI &gt; 50% col or row</th>
</tr>
</thead>
</table>
Results: PCLM

- **ANCOVA:**
  - were no significant statistical differences between groups at any time point for the composite scores

- **RMANOVA:**
  - improvement in each measurement over time for both groups for composite scores

- **PCL-M score for clinical changes for RROI**
  - 5-9 point score change demonstrates reliable change
  - 10 or greater score change demonstrates significant change
Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial – UHM 42 (4) 2015
E. George Wolf, Laura M. Baugh, Christine M. Schubert Kabban, Michael F. Richards, Jennifer Prye

- Concussion items
  - PCL-M had significant change in subjects with:
    - more than one concussive event
    - additional multiple non-concussive events
    - initiation of hyperbaric exposures within two years of last concussion
    - an impact etiology
  - Congruent with PTSD as a result of one or more life threatening events
Conclusion

- No significant statistical difference between a sham and HBO at 2.4 ATA in scores from ImPACT, Braincheckers or PCL-M
- Both groups showed improvement in scores
  - Theme for results from all DoD pilot studies thus far
  - Attributed to placebo effect
- Subgroups identified that responded to treatment vs sham
- Hydrostatic pressure has therapeutic findings
  - gene uploading/downloading
  - endothelial cell proliferation
  - Increased neuronal excitability
Conclusion

• HBOT appeared safe at a relatively high treatment pressure in chronic TBI subjects
• Data can be used to weigh the risk/benefit consideration when treating TBI patients
  • Definitive data still required
• Per AHRQ, the standard of proof of HBOT efficacy should be lowered
Hypotheses

- PTSD symptoms may respond to HBO₂ treatment
- In those with mTBI who seem to respond to HBO₂ - this response may be due to treatment of concomitant PTSD - rather than mTBI
- Ad Hoc analysis
  - Segregate subjects with PCL-M score >50
  - Analyze those who demonstrated a significant score decrease between treatment and sham groups
PTSD Symptoms

Percentage with **10 or more points** improvement in PCL-M Scores*

- **SHAM** (N=12): 33%
- **HBO2** (N=13): 77%

*p=0.028, Chi-Square, 1 DF

† Analysis limited to the “mTBI with PTSD” group
Percentage of subjects responding to therapy pooled data - USN and USAF
Increased circulating stem cells and better cognitive performance in traumatic brain injury subjects following hyperbaric oxygen therapy – UHM 44 (3) 2017
Sabrina Shandley, E. George Wolf, Christine M. Schubert-Kabban, et al

- Thom reported an increase in the number of CD34+ bone-marrow-derived stem/progenitor cells (SPCs) following HBO2
- Heyboer showed a potential dose-response relation in CD34+ and CD45-dim, with significant increases in patients treated at 2.5 ATA versus 2.0 ATA.
Increased circulating stem cells and better cognitive performance in traumatic brain injury subjects following hyperbaric oxygen therapy – UHM 44 (3) 2017
Sabrina Shandley, E. George Wolf, Christine M. Schubert-Kabban, et al

- Stem cells collected prior to series, after 15 exposures, after 30 exposure series, and 6 week post series.
- 13 subjects from 1.3 ATA air and 15 subjects from 2.4 ATA O₂
- Nestin is specifically associated with neuronal stem cells.
- CD34 represents a marker for hematopoietic and endothelial stem cells.
- CD₁₃₃ identified as a marker expressed on hematopoietic stem cells, neural and muscle progenitor cells.
Increased circulating stem cells and better cognitive performance in traumatic brain injury subjects following hyperbaric oxygen therapy – UHM 44 (3) 2017
Sabrina Shandley, E. George Wolf, Christine M. Schubert-Kabban, et al

Image Description:
- Two scatter plots are shown:
  - **HBOT**:
    - X-axis: Change in CD3+CD133+ from baseline to follow-up
    - Y-axis: Change in verbal memory from baseline to follow-up
    - Points represent data points following HBOT therapy.
  - **Sham**:
    - X-axis: Change in CD3+CD133+ from baseline to follow-up
    - Y-axis: Change in verbal memory from baseline to follow-up
    - Points represent data points following Sham therapy.
Increased circulating stem cells and better cognitive performance in traumatic brain injury subjects following hyperbaric oxygen therapy – UHM 44 (3) 2017
Sabrina Shandley, E. George Wolf, Christine M. Schubert-Kabban, et al

- Treatment CD 34+ or nestin are likely factors in the ImPACT and Braincheckers cognitive changes, but not CD 133+
- CD 133+ is likely the primary stem cell responsible for the PCL-M composite score changes.
- The sham group did not show any statistically significant correlations.
Dawn of a New Day

- Oklahoma: Veterans Traumatic Brain Injury Care Improvement Act of 2014
- Indiana: Chapter 13.5. Grants for Veterans' Services
  - Passed effective 1 July 17
  - Service related event within the past 12 months
  - Must pay 10% co-pay of the treatment cost billed
- Texas: Veterans Recovery Pilot Program
  - Provide Veterans with hyperbaric oxygen treatment
  - Passed 29 May 17; effective 1 Sep 17
Comments

• All DoD and civilian published studies have been PILOT STUDIES – safety, efficacy, and focus areas
• Current HBOT indications: only 3 of 14 are primary – all others are adjunctive therapy to standard of care
• HBOT for TBI or PTSD has NEVER been proposed as a primary treatment
• Development of a treatment registry needed
  • Consider criteria (time, cognitive tests, PTSD)
  • Conduct exposures in local areas (study experience)
  • Collect data from variety of exposures vs SOC+crossover
  • Define multiple outcome measures by clinicians