SCUBA and SCI in Paralyzed Veterans:
“There is a tide in the affairs of men,
Which taken at the flood,
leads on to fortune.”

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Disclosures

• Daniel Becker, MD
  Has no financial interest or relationships to disclose

• Adam Kaplin MD, PhD
  Has no financial interest or relationships to disclose
Subject Demographics

- Average time since SCI = 15 (range 4-33) years
- Average age = 37 (range 23-52) years old
- Sex = 9 male, 1 female.
- SCUBA Certification Dives = 8/10
- Asia Classification of SCI: 6xA, 2xB 1xC, 1xD
- SCUBA Certification
  - 10 Open Water Dives
  - Average Depth = 51 (range 15-99) feet
  - Average Time = 33 (range 21-45) minutes
Impact of Event Scale (PTSD Symptoms)

Subject 11  -92
Subject 18  -91
Subject 1   -87
Subject 13  -100
Subject 2   -57
Average     -78

Percent Change (Post/Pre/Pre)
PTSD is Generally Thought to Be Intractable in War Veterans

• Repeated SCUBA diving led to a near complete or complete resolution of PTSD symptoms in all of the paralyzed vets who manifested any initial symptoms.

• Could scuba be a novel therapy for PTSD?

• Possible Contributions:
  – Controlled Breathing
  – Mastering Fearful Situation
  – Pressure of Diving
  – CNS Changes as a Result of SCUBA
This review presents recent clinical trials and recent advances in the development of strategies to restore locomotion after SCI. Several approaches toward functional recovery in SCI succeeded in acute and subacute phases in animal models. However, effective strategies against chronic phase of SCI have not been established yet.
Standard of Care for Chronic SCI

• There is extensive and varied research currently underway on many different potential restorative therapies for Spinal Cord Injury, including FES.

• Currently there is no standard of care to restore function in chronic phase of SCI.

• What Neurological changes occurred with SCUBA?
SCUBA Background

• In a randomized, placebo-controlled, double-blind study Fischer et al (1983) reported improved spasticity in subjects treated with hyperbaric oxygen (2 ATA, 90 minutes daily, 5 days a week, total 20 treatments).

• Madorsky (1988) suggest that SCUBA diving could be a beneficial adjunct neuro-rehabilitative therapy for people with paraplegia.

• Stanghelle et al (1991) concluded that SCUBA diving is not unsuitable for patients with spinal cord injuries, even for tetraplegics. They also observed improved spasticity.
SCUBA Background

• Novak et al (1999) reported increased vital capacity after 2 weeks of SCUBA diving in 9 paraplegic subjects. A comparison group of subjects who were sailing for 2 weeks did not show these changes.

• In a 7 day trial (1 dive, 30 minutes per day at 23 feet) with 6 paraplegic subjects (traumatic and non-traumatic) Haydn et al (2007) reported significantly improved spasticity and improved quality of life in addition to improved pain. This effect persisted for less than 4 weeks.
  • Water temperature 52 to 61 F
  • Effect was observed after 3 days
  • Recommendation to repeat this study in warmer water and to provide SCUBA as “therapy” every 14-21 days
Reported Subjective Changes

• Improved spasticity
• Increased strength
• Improved balance
• Improved fatigue
• Improved breathing function
• Improved bladder sensation
• Improved bowel program
• Better sleep
• Decreased headache frequency
Spasticity

• Upper extremities (UE):
  – 3 subjects had UE spasticity at baseline (modified Ashworth scores 14-16)
  – All subjects improved
    • 2 normalized (score of 12)
    • 1 improved to 13
Spasticity Upper Extremities Percent Change  (p = 0.1181)

Subject 9
-7

Subject 18
-14

Subject 2
-25

Avg % Change
-15

Ashworth UE

SCI  Control  SCI Max  Control Max

p = 0.06
Lower extremities (LE):
  - All subjects had LE spasticity at baseline (modified Ashworth scores 14-58)
  - All but 1 subject improved by 7-28%
Spasticity Lower Extremities Percent Change

Subject 9: -13
Subject 11: -10
Subject 15: -18
Subject 18: -28
Subject 13: -23
Subject 4: -12
Subject 2: -7
Avg % Change: -16
Subject 10: 9

Ashworth LE

p = 0.001
Spasticity

• SCUBA Universally Improved Spasticity in Paraplegic Vets with SCI.
• These changes were only seen in those Vets who underwent SCUBA certification.
Pinprick (ASIA testing)

- Sensation to pinprick improved most in subjects with incomplete SCI (1-8 points).
Pin Prick Score Percent Change

Subjects: Subject 9, Subject 11, Subject 15, Subject 18, Subject 1, Subject 13, Subject 4, Subject 2, Subject 10, Subject 16

- Subject 9: 4
- Subject 11: 0
- Subject 15: 0
- Subject 18: 14
- Subject 1: -7
- Subject 13: 7
- Subject 4: 7
- Subject 2: 11
- AVG % Change: 4.5
- Subject 10: 0
- Subject 16: 4

ASIA PP

Post-Pre Score

p = 0.05
Light touch (ASIA testing)

- Sensation to light touch improved most in subjects with incomplete SCI (1-16 points).
**Light Touch Score Percent Change**

![Bar chart showing the percent change in light touch scores for different subjects.](image)

- **Subjects**: Subject 9, Subject 11, Subject 15, Subject 18, Subject 1, Subject 13, Subject 4, Subject 2, AVG % Change, Subject 10, Subject 16
- **Values**: 3, 0, 2, 2, 20, 20, 20, 9, 1, -5

*Inset graph showing post-pre score comparison with p = 0.001.*
Sensation

• The majority of Paraplegic Vets demonstrated improved sensation in either pin-prick, light touch or both.
• The improvements were selective for those who underwent SCUBA certification.
• All subjects who had incomplete motor function in either UE or LE demonstrated strength improvements from 1 to 10 points
Motor Score Percent Change

<table>
<thead>
<tr>
<th>Subject</th>
<th>Avg % Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 9</td>
<td>2</td>
</tr>
<tr>
<td>Subject 11</td>
<td>0</td>
</tr>
<tr>
<td>Subject 15</td>
<td>0</td>
</tr>
<tr>
<td>Subject 18</td>
<td>6</td>
</tr>
<tr>
<td>Subject 1</td>
<td>0</td>
</tr>
<tr>
<td>Subject 13</td>
<td>0</td>
</tr>
<tr>
<td>Subject 4</td>
<td>17</td>
</tr>
<tr>
<td>Subject 2</td>
<td>8</td>
</tr>
<tr>
<td>AVG % Change</td>
<td>4</td>
</tr>
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</table>

Inset: ASIA Motor

- SCI: p = 0.02
Motor Function

• Half of Paraplegic Subjects regained some motor function.
• These effects were selective for whose who underwent SCUBA certification.
Other Results

• Pulmonary Function tests
  – No change in Peak Flow in all groups

• Finger flexor strength (Grip Dynamometer)
  – Slight negative trend in all subjects without difference between groups

• Urine Output:
  – Virtually all subjects reported increased frequency and urine volume (42% – 51%) without differed between groups
Medical Complications Observed

- Skin injuries during transfers in and out of boat were the most frequent complaint
- Coral Injuries
- Jellyfish sting
- Ear decompression difficulty
- 1 Closed head injury (by ship ladder)
Plausible Mechanisms Whereby SCUBA Could Enhance Motor and Sensory Fxn in Chronic SCI

• External Environment:
  – Buoyancy: permits use of weak muscles
  – Water: global resistance training
  – Pressure: Temple Grandin & her squeeze machine

• Internal Environment:
  – Enhanced ventilation: better tissue gas exchange
  – Oxygen: oxygen therapy
  – Nitrogen: known CNS effects

• Neural Mechanisms: Rapid Response
  – Neural Adaptation with enhancement of existing circuits
  – Activation of preserved occult circuitry
Table 1. Neurologic Diseases Treated With Hyperbaric Oxygen

Stroke
Lower limb ischemia
Cerebral palsy
Increased intracranial pressure
Migraine headache
Brain injury
Radiation-induced necrosis
Hydrocephalus
Spinal cord injury
Pain, such as exercise-induced muscle soreness, decompression sickness, fibromyalgia syndrome, and complex regional pain syndrome

Table 3. Actions of Hyperbaric Oxygen in Neurologic Disease

Spinal cord injury
- Improves neurologic recovery
- Ameliorates mitochondrial dysfunction in the motor cortex and spinal cord
- Reduces micturitional disturbance and neurologic deficits
- Arrests spread of hemorrhage, reverses hypoxia, and reduces edema
- Resolves bone infection and helps wound healing in chronic osteomyelitis
Hyperbaric Oxygen Therapy

• Most of work in the treatment of acute SCI with HBO is anecdotal, but results are overall mixed and disappointing.
• Very little published on HBO in chronic SCI.
• So if not pressure and O2, what is it that is unique to SCUBA?
I am personally quite receptive to nitrogen rapture. I like it and fear it like doom. It destroys the instinct of life. Tough individuals are not overcome as soon as neurasthenic persons like me, but they have difficulty extricating themselves. Intellectuals get drunk early and suffer acute attacks on all the senses, which demand hard fighting to overcome. When they have beaten the foe, they recover quickly. The agreeable glow of depth rapture resembles the giggle-party jags of the nineteen-twenties when flappers and sheiks convened to sniff nitrogen protoxide.
Effects of nitrogen on extracellular level of dopamine, serotonin, glutamate and aspartate in rat

**Dopamine**

![Graph showing dopamine levels](image)

**Serotonin**

![Graph showing serotonin levels](image)

**Glutamate**

![Graph showing glutamate levels](image)

**Aspartate**

![Graph showing aspartate levels](image)

**FIGURE 3** – Development of dopamine, glutamate, serotonin and aspartate levels recorded by microdialysis in the striatum of rats exposed to 3 MPa of nitrogen-oxygen pressure. (U-Mann Whitney test * P<0.05; ** P<0.2; *** P<0.001).
Effects of Nitrogen on CNS

• Nitrogen is known to effect the CNS and cause Nitrogen Narcosis or Rapture of the Deep.
• In addition to the relatively moderate changes in glutamate and GABA in the CNS that account for its intoxicating effects, there is a dramatic 350% increase in CNS Serotonin.
• What do we know about the effect of Serotonin on the Spinal Cord?
• What role does Serotonin play in development, injury, and recovery?
Serotonin is Critical for CPG Development

- 5-HT induces rhythmic activity *in vitro* in Embryonic Mouse Spinal Cords
- By E18 coupled, alternating segmental pattern is mediated by 5-HT stimulation and transition of interneuronal GABA/Gly to inhibitory, which is affected by 5-HT.
Serotonin is Critical for CPG Development

- 5-HT induces locomotor activity in Early Neonatal Mouse Spinal Cords \textit{in vitro}.
- Blockade of D1/D2 Dopamine Receptors interferes with 5-HT evoked pattern.
- In Neonatal Mice Glutamate (NMDA) elicits rhythmic locomotor activity.
- NMDA antagonist change 5-HT+Dopamine induced rhythm but don’t block them.
- Thus, 5-HT effects on locomotion become supplemental later in development.
The Unusual Response of Serotonergic Neurons after CNS Injury: Lack of Axonal Dieback and Enhanced Sprouting within the Inhibitory Environment of the Glial Scar.
Serotonin Release Variations During Recovery of Motor Function After a Spinal Cord Injury in Rats

- Rat Spinal Cords were partially transected at T9
- Treadmill exercise on days 8, 18, 34 after lesion.
- Microdialysis measure of 5-HT release in Ventral Horn at L5.
- Levels of 5-HT increased 300% on day 18 that correlated with regaining function.
5-HT$_{1A}$ receptors are involved in short- and long-term processes responsible for 5-HT-induced locomotor function recovery in chronic spinal rat

Quipazin = 5-HT2 agonist

8-OHDPAT = 5-HT1a agonist

Serotonin 5-HT$_2$ receptor activation induces a long-lasting amplification of spinal reflex actions in the rat

5-HT in a neonatal rat preparation mediated a long-lasting facilitation of reflexes that could be maintained for several hours.

Some dorsal horn neurons underwent long-lasting facilitation of afferent-evoked EPSPs.

Thus, the increase in reflex gain coincides with an increase in sensory gain to a subpopulation of neurons.
Serotonin in the Spinal Cord

• 5-HT is central to the core development of the Spinal Cord Central Pattern Generator (CPG).
• Serotonergic neurons are selectively preserved in the CNS after injury.
• Correlating with the improvement in locomotion following SCI is the increased release in the Ventral Horn of 5-HT by 300%.
• Repeated stimulation of 5-HT receptors results in the rehabilitation of locomotion and following SCI.
• 23 year old who suffered C7-T1 SCI by MVA.
• Epidural spinal stimulator placed over L1-S1.
• Report after 80 standing sessions over 7 months with stimulation lasting 40-120 min.
• Patient was able to stand with full weight bearing with assistance for balance while stimulation was on.
Conclusions

• There is a need for restorative treatments for chronic spinal cord injured (SCI) individuals.
• No systematic studies have been done of SCUBA in SCI.
• We saw unprecedented improvement in motor and sensory function in paraplegic war veterans after undergoing four days of 9 successive SCUBA dives.
• SCUBA diving is known to increase CNS nitrogen levels, which in turn generate large increases in serotonin (5-HT) release within the central nervous system.
• Though never tested in humans, serotonin has been shown in animals to stimulate motor and sensory recovery in the context of spinal cord injury in animals.
• This pilot study suggests a back door mechanism to awaken function in the chronically injured spinal cord.
• The proposed mechanism of SCUBA mediated improved function in Chronic SCI should be further investigated.
We Think This May Be of General Interest to Fitness Enthusiasts!
Acknowledgements

• Cody Unser
• Shelley Unser
• Al Kovach
• All PVA Participants & Dive Instructors
• Medical Team: Sheena Patel & Jeffrey Cheng
• Research Mechanisms: Kristen Rahn
• Chris Schueler and Film Crew
Obtaining CME Credit

• If you would like to receive CME credit for this activity, please visit:

http://www.pesgce.com/PVAsummit2011/

• This information can also be found in the Summit 2011 Program on page 8.


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ASIA PP

Post - Pre Score

SCI  |  Control  |  SCI Max  |  Control Max

p = 0.05
Ashworth UE

Post - Pre Score

p = 0.06

SCI
Control
SCI Max
Control Max
Spasticity Upper Extremities Percent Change (p = 0.1181)

- Subject 2: -25
- Subject 9: -7
- Subject 18: -14
- Avg % Change: -15
Spasticity Lower Extremities Percent Change

Subject 2: -7
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Subject 13: -23
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Avg % Change: 9

Subject 10: -16
Pin Prick Score Percent Change

- Subject 1: -7
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a The motor infrastructure

- **Spinal cord**: Protective reflexes, Locomotion
- **Cerebellum**: Fine motor control (speech, hand/finger coordination)
- **Basal ganglia**: Feeding, Drinking
- **Brainstem**: Respiration, Chewing, Swallowing, Eye movements

b The vertebrate control scheme for locomotion

- **Selection**: Forebrain
  - Basal ganglia
  - Feeding, Eye movements
- **Initiation**: Brainstem
  - DLR, MLR
  - Locomotion
- **Pattern generation**: Spinal cord
  - Central spinal network
  - Movement feedback
  - Pharmacological activation
  - Sensory activation
Fig. 1. Schematic representation of the role of hippocampal function in context fear memory. Here we suggest that a shift to a predominantly elemental strategy would allow elemental cues to have a much larger role in behavioral responses to the environment, with each discrete cue encoded during trauma able to induce conditioned fear responses across multiple contexts. The left side of the figure demonstrates how normal hippocampal function allows for the formation of a conjunctive context representation consisting of a combination of individual elements. This conjunctive representation is then associated with the traumatic event (in this case an exploding grenade). Upon later exposure to a single element of the original context (in this case the garbage bag), no fear response is triggered. The right side of the figure demonstrates how impaired hippocampal function precludes formation of a conjunctive representation. Instead, each individual element of the context is independently associated with the traumatic event. Due to this single-element association, later exposure to only the garbage bag (independent of other contextual elements) is then sufficient to trigger a fear response.
Effects of nitrogen on extracellular level of dopamine, serotonin, glutamate and aspartate in rat

**Dopamine**

![Dopamine Graph]

**Serotonin**

![Serotonin Graph]

**Glutamate**

![Glutamate Graph]

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