Deficient low-contrast visual sensitivity occurs in patients with multiple sclerosis: May degrade gait performance, possible modification utilizing high contrast visual aids.

Kelly Schwirian
Rachel Tripoli
Dr. C.G. Maitland
BACKGROUND & HYPOTHESIS


- The impact of deficient low contrast sensitivity has not yet been explained in patients with M.S. to any degree.
  - Since optic neuropathy is found in over 80% of patients with M.S., it seems prudent to investigate any mechanism that might improve the function of affected individuals.

- The application of high-contrast, blue-blocking yellow lenses was investigated in hopes of improving vision in low-contrast environments, and thus possibly allowing for better obstacle discrimination.
METHODODOLOGY

- Four parameters were used to stage the degree of pathology of patients with multiple sclerosis and age matched controls
  - Estimated Disability Severity Scale
    - Ten-point scoring system that evaluates visual, motor, brainstem, sensory, and cognitive dimensions of patients with M.S.
  - Low Contrast Sloan Letter Chart
  - Optical Coherence Tomography
  - Gait Pad Measurement
METHODOLOGY

- Patients tested with both eyes first, then right and left eye individually first at 100% efficiency, then at 2.5%, and then at 1.25% efficiency.

- The Snellen visual acuity equivalent will be determined by the lowest line read on the 100% chart.
To ensure a complete assessment of optic nerve topography, patients were examined using optical coherence tomography to assess thickness of the optic nerve fiber bundle.
METHODOLOGY

GaitRite Pad Measurement

- Patients were asked to walk on a 22 foot gait pad that measures 102 parameters of gait.

- The GaitRite pad (CIR Systems, Inc.) contains six sensor pads that extract readings from over 16,000 sensors embedded within a carpet that record patient data in an area 24 inches wide and 1400 inches long.

- Ambulation time, velocity, right and left footfall pressure and duration, and Functional Ambulation Performance (FAP) scores were calculated for each patient.

http://www.gaitrite.com/Products/index-new.html
Our study consisted of 22 MS patients and 22 age-matched controls

- **EDSS Assessment**
  - Evaluated on a scale of 0 – 10 based on disease progression

- **Visual Acuity**
  - Measured using the Sloan chart at 100%, 2.5%, and 1.25%
  - Contrast vision measured with both eyes, the right eye, and the left eye

- **OCT**
  - Used to measure optic nerve thickness
METHODOLOGY

- **GaitRite Pad**
  - 8 randomized walking trials per patient
    - 4 in high illumination (> 80 candela)
      - 2 with obstacles
        - 1 with lenses and 1 without
      - 2 without obstacles
        - 1 with lenses and 1 without
    - 4 in dim illumination (< 4 candela)
      - 2 with obstacles
        - 1 with lenses and 1 without
      - 2 without obstacles
        - 1 with lenses and 1 without

- **MEASUREMENTS**
  - Functional ambulation profile (FAP)
  - Step number, normalized velocity, step length, step length differential, stride length, and cadence
**Significant Findings**

*Evaluated using paired T-testing*

- Poorer contrast visual acuity in MS patients
  - Measured using the Sloan chart
  - Significant difference at 100%, 2.5%, and 1.25%

- MS patients had thinner optic nerves
  - Measured using OCT

- Thinner optic nerves correlated negatively with visual acuity
  - Patients with thinner optic nerves (measured using OCT) had poorer performance on the Sloan chart
SIGNIFICANT FINDINGS

- Visual deficiency significantly degraded motor performance in dim illumination
  - Especially seen with complicated walking (obstacles)
  - Significant differences seen in FAP, velocity, normalized velocity, cadence, step length, and stride length
  - No deficiency seen in high illumination

- Negative correlation between FAP and EDSS scores
  - MS patients with an EDSS score of 4 or less had significantly worse FAP scores than those with a score of 4 or greater

- Yellow lenses improved FAP scores of MS patients in dim illumination
  - Especially significant with complicated walking (obstacles)
  - No significant differences seen between MS patients and controls in dim illumination with lenses
CONCLUSION

- Contrast sensitivity deficits degrade motor performance in MS patients in dim illumination
  - These deficits are presumably the result of optic neuropathy
  - MS patients have decreased FAP scores
    - Low FAP scores correlate highly with increased fall risk

- High-contrast yellow lenses improve low-contrast vision in MS patients
  - These lenses increase obstacle discrimination, and could potentially result in a reduction in risk of injury from falls
REFERENCES


FUNDING FOR THIS RESEARCH PROVIDED BY:

- FSU College of Medicine
- TMH Foundation
Effects of Exogenous Melatonin Administration and its Role in Cognitive Function Among Elderly Subjects.

Rick Sims (M2)
Dr. Ken Brummel-Smith
Dr. James Olcese
Dr. Gerry Maitland
Alzheimer’s Disease

- Progressive disease that affects one’s memory, thinking, and behavior.
- No single mechanism, rather a multi-factorial progression leading to neuronal deterioration.
- Pathological Changes
  - Amyloid-beta plaques
  - Neurofibrillary tangles
  - Mitochondrial dysfunction characterized by Reactive Oxygen Species, decreased ETC
Treatment

- Cholinesterase Inhibitors – ACh
- Memantine – glutamate
- Melatonin
  - Animal studies show:\(^1\):
    - Reduction in ROS production and restoration of mitochondrial function
    - Long-term treatment reduced amyloid-beta plaque deposition and aggregation
Method

- **Hypothesis**
  - Melatonin at 15 mg/day will create measurable cognitive improvement in elderly subjects.
- **Double-blind placebo controlled trial**
- **N= 26**
  - Melatonin = 16
  - Control = 10
- **15mg Melatonin QHS x 42 days**
- **Subjects**
  - 66 and older
  - Mild Cognitive Impairment
- **Test: Montreal Cognitive Assessment (MoCA)**
## Results

<table>
<thead>
<tr>
<th></th>
<th>Melatonin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Value (pre-)</td>
<td>25.00</td>
<td>23.50</td>
</tr>
<tr>
<td>Median Value (post-)</td>
<td>27.00</td>
<td>25.00</td>
</tr>
<tr>
<td>Std. Deviation (pre-)</td>
<td>1.65</td>
<td>3.57</td>
</tr>
<tr>
<td>Std. Deviation (post-)</td>
<td>1.69</td>
<td>2.96</td>
</tr>
</tbody>
</table>
MoCA scores after 6 weeks

- Scores ranged from 15-30
- P value = 0.0950 (not statistically significant)
Adjusted MoCA scores

Scores ranged from 21-30
P value = 0.0341 (statistically significant)
Questions/Problems

• Prior Study\(^2\):
  – 1mg/night x 28 days
  – 26 healthy elderly patients
  – California Verbal Learning Test
  – Conclusion: “Melatonin administration at a dose of 1 mg nightly may be effective in improving certain aspects of cognitive functioning…”

• Duration
• Strength
• Exogenous Melatonin Levels
Future Directions

• 6 month study
• 15mg Melatonin QHS x 6 months
• N = 100

Questions?
Presence of dysphagia after anterior discectomy and fusion with a low-profile device

James E. Pilkington (M2)
Charles Wingo, M.D. (Faculty Advisor-Tallahassee Orthopedic Clinic)
January 5, 2012

Outline

• Introduction/Background
  ▪ Anterior cervical discectomy and fusion
    ❖ Anterior plating
    ❖ The Synthes® Zero-p

• Our research

• Future Research
Anterior cervical discectomy and fusion (ACDF)

Indication:
• Considered the “gold standard” surgical treatment for diseases of the cervical spine
  ▪ Degenerative disc disease
  ▪ Cervical spondylotic myelopathy
  ▪ Spinal stenosis
  ▪ Pseudoarthrosis
Anterior cervical discectomy and fusion (ACDF)

Procedure:
• Involves the removal of the vertebral disc and introducing a bone graft to replace the disc
• Results in a decompression of compressed nerves or spinal stenosis
ACDF with anterior plating

• An anterior plate is surgically fixated anteriorly to the vertebral bodies above and below the operated segment.

• Many surgeons add an anterior plate to increase the likelihood of fusion.
Complications of ACDF with anterior plating

- 2% to 67% of patients may complain of dysphagia in the early postoperative period.
- 3% to 21% of patients may complain of chronic dysphagia.
- Additionally, cases of soft-tissue damage due to migrating screws have been reported.
- Reports also show that anterior plating may be associated with higher rates of degeneration at adjacent levels.
ACDF with Synthes® Zero-p

Reasons for development

• To potentially avoid complications of ACDF with anterior plating while still maintaining the added stability

• It was modeled after a similar device used for the lumbar spine.
ACDF with Synthes® Zero-p

Indications

• Degenerative disc disease of the cervical spine
• Spinal stenosis
• Failed previous fusions
• Pseudoarthrosis

Contraindications

• Spinal fracture
• Spinal tumor
• Severe osteoporosis
• Spinal infection
• Spinal instability
ACDF with Synthes® Zero-p

Past research is limited to two studies by Scholz et al.

First study:
- Found that the Zero-p device had similar biomechanical stability to ACDF with anterior plating
ACDF with Synthes® Zero-p

Second study:

- Found that chronic dysphagia was infrequent when compared to published data from other ACDF methods
- Found visual analog pain scale scores and neck disability indices were reduced at six weeks follow up
- Found no incidences of device failure
Procedure

Scholz et al; *Clin Orthop Relat Res.* Vol 469, No. 3, 2011
Our Study

Reasoning

• Little research has been conducted on the effectiveness of the Zero-p device.

• Some insurance companies still view the procedure as “experimental.”
Our Study

Clinical questions
• Is the Zero-p device associated with low rates of dysphagia?
• Is the Zero-p device effective at reducing neck disability and pain?
• Is there any radiologic evidence of device failure or screw loosening at any time during postoperative follow up?
Methods

Participants: Male and female patients who underwent ACDF with Zero-p by Dr. Wingo at Capital Regional Medical Center between March 2009 and December 2010

Treatment: ACDF with Zero-p device and NovaBone grafting
Methods

Data collection:
• Structured phone interviews collected at least six months postoperatively (mean=16.88 months ± 5.43)
• Dr. Wingo analyzed radiographs for participants with at least six months follow up for evidence of fusion or device failure.
# Results – Preoperative data

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n=26)</th>
<th>Monosegmental ACDF (n=21)</th>
<th>Bisegmental ACDF (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.58 ± 10.93</td>
<td>54.5 ± 10.62</td>
<td>67 ± 5.35</td>
</tr>
<tr>
<td>Number of women</td>
<td>15</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Number of men</td>
<td>11</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>BMI</td>
<td>29.13 ± 5.75</td>
<td>29.96 ± 5.87</td>
<td>25.78 ± 4.20</td>
</tr>
<tr>
<td>NDI score</td>
<td>23.5 ± 12.22</td>
<td>25.94 ± 11.15</td>
<td>12.5 ± 12.01</td>
</tr>
<tr>
<td>Level C3/C4</td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Level C4/C5</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Level C5/C6</td>
<td>13</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Level C6/C7</td>
<td>7</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Total implants</td>
<td>31</td>
<td>21</td>
<td>10</td>
</tr>
</tbody>
</table>
Dysphagia rates

![Graph showing dysphagia rates at different time periods: Preoperative (15.38%), Postoperative (42.31%), 3 months (7.69%), and 6 months (3.85%).]
Dysphagia comparison

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Dysphagia short term (&lt; 2 months)</th>
<th>Dysphagia medium term (3-6 months)</th>
<th>Dysphagia long term (&gt; 6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wingo et al. (current study)</td>
<td>26</td>
<td>42.3%</td>
<td>7.7%</td>
<td>3.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Dysphagia comparison

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Dysphagia short term (&lt; 2 months)</th>
<th>Dysphagia medium term (3-6 months)</th>
<th>Dysphagia long term (&gt; 6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wingo et al.</td>
<td>26</td>
<td>42.3%</td>
<td>7.7%</td>
<td>3.9%</td>
</tr>
<tr>
<td>(current study)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scholz et al.</td>
<td>34</td>
<td>62%</td>
<td>2.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Dysphagia comparison

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Dysphagia short term (&lt; 2 months)</th>
<th>Dysphagia medium term (3-6 months)</th>
<th>Dysphagia long term (&gt; 6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wingo et al. (current study)</td>
<td>26</td>
<td>42.3%</td>
<td>7.7%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Scholz et al.</td>
<td>34</td>
<td>62%</td>
<td>2.9%</td>
<td></td>
</tr>
<tr>
<td>Yue et al.</td>
<td>74</td>
<td></td>
<td></td>
<td>35.1%</td>
</tr>
<tr>
<td>Smith-Hammond et al.</td>
<td>38</td>
<td>47.0%</td>
<td></td>
<td>23%</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>310</td>
<td>54.0%</td>
<td>18.6%</td>
<td>15.2%</td>
</tr>
<tr>
<td>Bazaz et al.</td>
<td>249</td>
<td>50.2%</td>
<td>17.8%</td>
<td>12.5%</td>
</tr>
</tbody>
</table>
Neck disability index

- Preoperative: Neck Disability Score
  - Std. dev. 12.22

- Postoperative: Neck Disability Score
  - Std. dev. 9.19

- Average Reduction: Neck Disability Score
  - Std. dev. 12.92
Visual analog pain scale

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>Average reduction in pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual analog pain scale score</td>
<td>8</td>
<td>2.37</td>
<td>5.42</td>
</tr>
<tr>
<td>Std. dev.</td>
<td>2.42</td>
<td>2.37</td>
<td>2.81</td>
</tr>
</tbody>
</table>

The visual analog pain scale score shows a significant reduction in pain after surgery, with a standard deviation of 2.37 postoperatively and 2.81 for the average reduction in pain.
Influence of number of surgical levels on presence of dypshagia

Number of patients

Number of patients

1 level

2 levels

No dysphagia

Dysphagia
Influence of neck disability on the presence of dysphagia post surgery

Level of neck disability before surgery

Number of patients

<table>
<thead>
<tr>
<th>Level of Neck Disability</th>
<th>No dysphagia</th>
<th>Dysphagia</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Moderate</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Complete</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>
Results - Radiographs

• Examination of radiographs revealed no evidence of device failure or screw loosening in any patient.
• 100% assurance of solid fusion was only seen in 1 patient with x-ray.
• CT scan is the best indicator of fusion and was not performed on any patient postoperatively.
Conclusions

• ACDF with Zero-p is effective in reducing neck disability and pain in the cervical spine with low rates of device failure or complications.

• Postoperative chronic dysphagia rates are lower than that of published data.
Future research

• Prospective randomized-control study at multiple sites to confirm observations
• Larger sample size
• Longer follow up
• Perform radiographic studies including CT scan at six months follow up
Acknowledgements

• Dr. Charles Wingo
• Ms. Lisa Alwine

• FSU College of Medicine Research Fellowship
• FSU College of Medicine Seed Grant
References


References (cont.)


Questions?

Laboring to Understand the Circadian Contribution to Myometrial Excitability in Late Term Pregnancy

Courtney Paradise
Mentor: Dr. James Olcese
Study Aims

- Understand the reaction of the uterus to melatonin during late term pregnancy (>37th week)

- Elucidate the biological mechanisms that are responsible for the initiation of uterine contractions

- Gain a better understanding of the regulation and control of the myometrium in pregnancy to facilitate future clinical interventions in preterm labor
Rationale

- Preterm births represent one of the main causes of infant mortality and delivery complications

- To date, minimal progress has been made in regards to the mechanism of action that is responsible initiating term and preterm labor

- Therefore, there is a significant need for additional research on the subject of labor initiation in order to improve maternal and newborn health outcomes
Background

- The myometrium is stimulated by factors such as prostaglandins, norepinephrine, and oxytocin

- Several studies have shown that the majority of pregnant women go into labor in the night/early morning hours

- This suggests a correlation between uterine contractions and circadian fluctuations

- Melatonin (MEL) is a brain hormone responsible for signaling circadian night to the body

- Recently, a novel interaction between MEL receptors and oxytocin receptors on the myometrium has been identified by Dr. James Olcese and his team
A) MEL significantly potentiates oxytocin (OT)-induced contractions of human myometrial smooth muscle cells

B) Specific MEL receptor blockers reduce myometrial smooth muscle cell contractions

Design and Methods

- Participants for the study are in their last weeks of pregnancy (>37 weeks)
- They are connected to a tocometer (a device that measures the force of uterine contractions), and blood is collected at hourly intervals from 7 PM to 7 AM
- Uterine contractile activity and MEL blood levels are monitored throughout the night for each patient
- Lighting in the room is kept dim to facilitate MEL release
- At 11 PM a 10,000 lux light source is positioned approx. 70 cm away from the participants head for one hour
Fig. 1: This graph represents the expected effects of light exposure on MEL secretion and uterine contractions (UtC). During the circadian dark cycle, MEL levels should decrease upon exposure to light, and as a result, UtC should subside.
Fig. 2: Frequency of nocturnal contractions in a late term pregnant human volunteer as assessed during the night. At 11:00 pm (arrow) the subject was exposed to bright light.
Nocturnal uterine contraction frequencies and serum melatonin levels in late term pregnant women before, during and after exposure to bright light

<table>
<thead>
<tr>
<th>Time of collection</th>
<th>Contractions per hr</th>
<th>Contractions per hour</th>
<th>Melatonin percent of maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-8 p.m.</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8-9 p.m.</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9-10 p.m.</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10-11 p.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11-12 p.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12 a.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-2 a.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2-3 a.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3-4 a.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4-5 a.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5-6 a.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6-7 a.m.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Representative tocometric tracing and criteria for contractions (*)

[Graphs and data]
References
