Meta-analysis of self-control study: Methods and associated application of METAN

Dr. Robert Borotkanics, DrPH, MS, MPH
Research Fellow, Faculty of Medicine and Health Sciences
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REVIEW

Abdominal functional electrical stimulation to improve respiratory function after spinal cord injury: a systematic review and meta-analysis

This article has been corrected since Advance Online Publication and a corrigendum is also printed in this issue.

EJ McCaughey¹, RJ Borotkanics¹,², H Gollee³,⁴, RJ Folz⁵ and AJ McLachlan⁶

Objectives: Abdominal functional electrical stimulation (abdominal FES) is the application of a train of electrical pulses to the abdominal muscles, causing them to contract. Abdominal FES has been used as a neuroprosthesis to acutely augment respiratory function and as a rehabilitation tool to achieve a chronic increase in respiratory function after abdominal FES training, primarily focusing on patients with spinal cord injury (SCI). This study aimed to review the evidence surrounding the use of abdominal FES to improve respiratory function in both an acute and chronic manner after SCI.

Settings: A systematic search was performed on PubMed, with studies included if they applied abdominal FES to improve respiratory function in patients with SCI.

Methods: Fourteen studies met the inclusion criteria (10 acute and 4 chronic). Low participant numbers and heterogeneity across studies reduced the power of the meta-analysis. Despite this, abdominal FES was found to cause a significant acute improvement in cough peak flow, whereas forced exhaled volume in 1 s approached significance. A significant chronic increase in unassisted vital capacity, forced vital capacity and peak expiratory flow was found after abdominal FES training compared with baseline.

Conclusions: This systematic review suggests that abdominal FES is an effective technique for improving respiratory function in both an acute and chronic manner after SCI. However, further randomised controlled trials, with larger participant numbers and standardised protocols, are needed to fully establish the clinical efficacy of this technique.

Spinal Cord advance online publication, 12 April 2016; doi:10.1038/sc.2016.31
The research question

“Is AFES an effective intervention to improve respiratory function in both an acute and chronic manner after SCI?”

Spinal cord injury with paralysis is a low prevalence condition:
• Impaired function of respiratory muscles
• Atelectasis, pneumonia or ventilator failure are primary causes of morbidity and mortality

Abdominal functional electrical stimulation (AFES) trials:
• Application of a train of electrical pulses to motor nerves, causing contraction
Methodological considerations

1. Multiple measures of function

2. Self control studies or controlled trials

3. Different study approaches
   - Acute: quantification of function during AFES
   - Chronic: Quantification of function

4. Small study sizes: 4 – 24 subjects

5. Repeated treatments
Methodological framework: acute and chronic

Fixed effects (inverse of the variance)

Random effects (DerSimonian & Laird)

I^2

<0.3

> 0.3

Standardized mean difference

Glass’s $\Delta = \mu1 - \mu2/\sigma2$

(stratified analyses for chronic and function)

Publication bias
(Begg & Muzumdar; Eggar)
Meta-analysis in Stata using Metan

• Technical bulletins, 1998-2000
• More technical bulletins, 2001-2009
• *Meta-Analysis in Stata: An Updated Collection from the Stata Journal*, 1st Ed., 2009
• Technical bulletins, 2010-2016
• *Meta-Analysis in Stata: An Updated Collection from the Stata Journal*, 2nd Ed., 2016

‘update all’
‘search meta’
Flexible and powerful:

- Relative risk, odds ratios, differences in means, standardized differences in means
- Fixed or random effects
- Automatically generates forest plots

Has many options; can get complicated quite quickly

Basic construction:

```
metan varlist [if] [in] [,
    [binary_data_options|continuous_data_options|precalculated_effect_estimates_options]
    measure_and_model_options output_options forest_plot_options ]
```

Bradburn, et al., 1998; Harris, et al., 2008
Canonical, continuous effect measure:
‘metan Ynosubjects Ymean Ysd Xnosubjects Xmean Xsd, options

Basic example:
‘metan nopatients blmean1 blsd1 nopatients postmean postsd, lcols(study nopatients) glass by(measure)’

More complex:
‘metan nopatients postmean postsd nopatients blmean blsd, glass (by measure) sgweight lcols(study blmean blsd postmean postsd nopatients) favours(Favours Control # Favours Treatment) textsize(135) astext(75) diamopt(lcolor(black) lwidth(thin)) boxopt(mcolor(gs12)) ciopt(lwidth(thin)) olineopt(lcolor(gs12) lwidth(thin) lpattern(dash))’
Results: acute (snippet)
### Results: acute (snippet 02)

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline Mean (cmH₂O)</th>
<th>Baseline SD</th>
<th>AFES Mean (cmH₂O)</th>
<th>AFES SD</th>
<th>Total Participants</th>
<th>SMD (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butler²</td>
<td>19.50</td>
<td>6.00</td>
<td>57.90</td>
<td>7.00</td>
<td>11</td>
<td>5.89 (3.88, 7.90)</td>
<td>51.43</td>
</tr>
<tr>
<td>McBain¹⁵</td>
<td>1.90</td>
<td>0.60</td>
<td>37.10</td>
<td>2.00</td>
<td>15</td>
<td>23.84 (17.56, 30.13)</td>
<td>48.57</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>15</strong></td>
<td>14.61 (-2.98, 32.19)</td>
<td><strong>100.00</strong></td>
</tr>
<tr>
<td>(I-squared = 96.5%, p = 0.000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butler²</td>
<td>31.20</td>
<td>8.70</td>
<td>56.60</td>
<td>10.50</td>
<td>11</td>
<td>2.63 (1.47, 3.80)</td>
<td>51.31</td>
</tr>
<tr>
<td>McBain¹⁵</td>
<td>8.90</td>
<td>1.10</td>
<td>35.40</td>
<td>2.70</td>
<td>15</td>
<td>12.85 (9.41, 16.30)</td>
<td>48.69</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>15</strong></td>
<td>7.61 (-2.40, 17.62)</td>
<td><strong>100.00</strong></td>
</tr>
<tr>
<td>(I-squared = 96.7%, p = 0.000)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**NOTE:** Weights are from random effects analysis
### Table 2: Longitudinal effect of abdominal FES training on respiratory function between baseline and conclusion of treatment

<table>
<thead>
<tr>
<th>Measure</th>
<th>Author</th>
<th>Modality</th>
<th>Participants</th>
<th>SMD</th>
<th>CI</th>
<th>Weight</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (l)</td>
<td>Cheng\textsuperscript{14}</td>
<td>Stim</td>
<td>13</td>
<td>0.786</td>
<td>-0.045 to 1.616</td>
<td>29.93</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McBain\textsuperscript{15}</td>
<td>Stim</td>
<td>15</td>
<td>0.213</td>
<td>-0.507 to 0.933</td>
<td>39.82</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McLachlan\textsuperscript{10}</td>
<td>Stim</td>
<td>12</td>
<td>0.491</td>
<td>-0.335 to 1.317</td>
<td>30.26</td>
<td></td>
</tr>
<tr>
<td>I-V pooled SMD ($\bar{R} = 0.00$, df=2, $P=0.593$)</td>
<td>Cheng\textsuperscript{14}</td>
<td>Control</td>
<td>13</td>
<td>0.469</td>
<td>0.014 to 0.923</td>
<td>0.043</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cheng\textsuperscript{14}</td>
<td>Stim</td>
<td>13</td>
<td>0.05</td>
<td>-0.719 to 0.819</td>
<td>0.899</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McBain\textsuperscript{15}</td>
<td>Stim</td>
<td>15</td>
<td>0.786</td>
<td>-0.045 to 1.616</td>
<td>45.19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McLachlan\textsuperscript{10}</td>
<td>Stim</td>
<td>15</td>
<td>0.642</td>
<td>-0.112 to 1.396</td>
<td>54.81</td>
<td></td>
</tr>
<tr>
<td>I-V pooled SMD ($\bar{R} = 0.00$, df=1, $P=0.802$)</td>
<td>Cheng\textsuperscript{14}</td>
<td>Control</td>
<td>13</td>
<td>0.12</td>
<td>-0.650 to 0.890</td>
<td>0.760</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cheng\textsuperscript{14}</td>
<td>Stim</td>
<td>13</td>
<td>0.314</td>
<td>-0.465 to 1.093</td>
<td>32.46</td>
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</tr>
<tr>
<td></td>
<td>McBain\textsuperscript{15}</td>
<td>Stim</td>
<td>15</td>
<td>0.258</td>
<td>-0.464 to 0.981</td>
<td>37.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McLachlan\textsuperscript{10}</td>
<td>Stim</td>
<td>12</td>
<td>0.35</td>
<td>-0.463 to 1.163</td>
<td>29.77</td>
<td></td>
</tr>
<tr>
<td>I-V pooled SMD ($\bar{R} = 0.00$, df=1, $P=0.986$)</td>
<td>Cheng\textsuperscript{14}</td>
<td>Control</td>
<td>13</td>
<td>0.304</td>
<td>-0.140 to 0.748</td>
<td>0.180</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cheng\textsuperscript{14}</td>
<td>Stim</td>
<td>13</td>
<td>0.12</td>
<td>-0.650 to 0.890</td>
<td>0.760</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McBain\textsuperscript{15}</td>
<td>Cough</td>
<td>15</td>
<td>0.431</td>
<td>-0.302 to 1.165</td>
<td>39.61</td>
<td></td>
</tr>
<tr>
<td></td>
<td>McLachlan\textsuperscript{10}</td>
<td>Stim</td>
<td>12</td>
<td>0.18</td>
<td>-0.624 to 0.983</td>
<td>32.98</td>
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</tr>
<tr>
<td>I-V pooled SMD ($\bar{R} = 12.4$, df=2, $P=0.319$)</td>
<td>Cheng\textsuperscript{14}</td>
<td>Control</td>
<td>13</td>
<td>0.526</td>
<td>-0.064 to 1.987</td>
<td>0.026</td>
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</tr>
<tr>
<td></td>
<td>Cheng\textsuperscript{14}</td>
<td>Stim</td>
<td>13</td>
<td>0.968</td>
<td>0.107 to 1.828</td>
<td>46.36</td>
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</tr>
<tr>
<td></td>
<td>McLachlan\textsuperscript{10}</td>
<td>Stim</td>
<td>12</td>
<td>0.00</td>
<td>-0.800 to 0.800</td>
<td>53.64</td>
<td></td>
</tr>
<tr>
<td>D-L pooled SMD ($\bar{R} = 61.6$, df=1, $P=0.107$)</td>
<td>Cheng\textsuperscript{14}</td>
<td>Control</td>
<td>13</td>
<td>0.47</td>
<td>-0.478 to 1.418</td>
<td>0.134</td>
<td></td>
</tr>
</tbody>
</table>

McCaughey, et al., 2016
Conclusions

• A more nuanced approach is required to the meta-analysis of self-control studies
• Existing methods can be adapted to address these nuances
• Stata’s user-developed metan command enables meta-analysis of such study designs