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

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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 McCaughey[1], RJ Borotkanics[1,2], H Gollee[3,4], RJ Folz[5] and AJ McLachlan[6]

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

I^2

<0.3 **> 0.3**

Fixed effects
(inverse of the variance)

Standardized mean difference

Random effects
(DerSimonian & Laird)

Glass's $\Delta = \mu 1 - \mu 2 / \sigma 2$

(stratified analyses for chronic and function)

Publication bias
(Begg & Muzumdar; Eggar)

Meta-analysis in Stata using Metan

- Technical bulletins, 1998-2000
- *Meta-analysis in Stata*, JAC Sterne, MJ Bradburn, M Egger, within Systematic Reviews in Health care, 2001, Egger, et al., (eds.)
- 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'

METAN

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

METAN (cont.)

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:

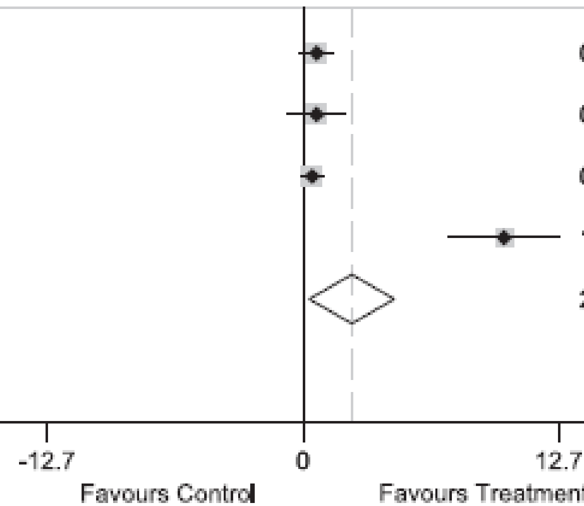
‘metan nopatients postmean postsd nopatients blmean blsd, glass (by measure) sgweight lcols(study blmean blsd postmean postsd nopatients) favours(Favours Control # Favours Treatment) textsize(135) astext(75) diamopt(lcolor(black) lwidth(thin)) boxopt(mcolor(gs12)) ciopt(lwidth(thin)) olineopt(lcolor(gs12)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

Results: acute (snippet)

a

Study	CPF Baseline Mean (L/s)	CPF Baseline SD	CPF AFES Mean (L/s)	CPF AFES SD	Total Participants	SMD (95% CI)	Weight (%)
Butler[2]	3.01	1.34	4.00	1.53	11	**0.69 (-0.17, 1.55)**	**27.32**
Gollee[3]	1.94	0.91	2.70	1.29	4	**0.68 (-0.76, 2.12)**	**25.25**
Jaeger[4]	3.38	0.87	3.83	1.07	24	**0.46 (-0.11, 1.04)**	**28.03**
McBain[15]	2.10	0.10	3.10	0.10	15	**10.00 (7.28, 12.72)**	**19.40**
Overall (I-squared = 93.4%, p = 0.000)						**2.43 (0.32, 4.54)**	**100.00**

NOTE: Weights are from random effects analysis



McCaughey, *et al.*, 2016

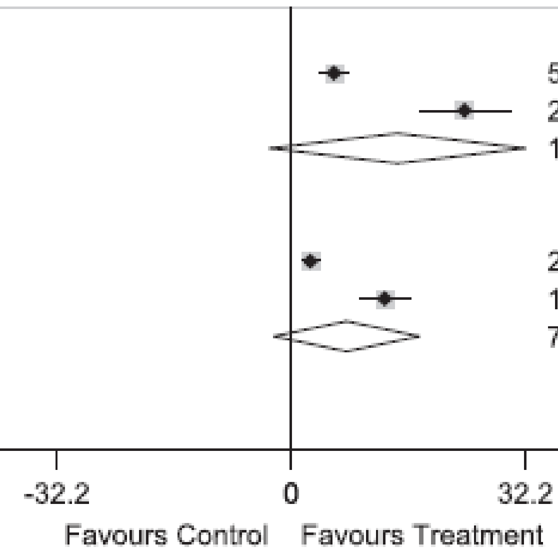
Results: acute (snippet 02)

MACQUARIE University

b

Study	Baseline Mean (cmH_2O)	Baseline SD	AFES Mean (cmH_2O)	AFES SD	Total Participants	SMD (95% CI)	Weight (%)
Pga (cough)							
Butler[2]	19.50	6.00	57.90	7.00	11	5.89 (3.88, 7.90)	51.43
McBain[15]	1.90	0.60	37.10	2.00	15	23.84 (17.56, 30.13)	48.57
Subtotal (I-squared = 96.5%, p = 0.000)						14.61 (-2.98, 32.19)	100.00
Pes (cough)							
Butler[2]	31.20	8.70	56.60	10.50	11	2.63 (1.47, 3.80)	51.31
McBain[15]	8.90	1.10	35.40	2.70	15	12.85 (9.41, 16.30)	48.69
Subtotal (I-squared = 96.7%, p = 0.000)						7.61 (-2.40, 17.62)	100.00

NOTE: Weights are from random effects analysis



Results: chronic (snippet)

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Table 2 Longitudinal effect of abdominal FES training on respiratory function between baseline and conclusion of treatment

Measure	*Author*	*Modality*	*Participants*	*SMD*	*CI*	*Weight*	*P-value*
FVC (l)	Cheng[14]	Stim	13	0.786	−0.045 to 1.616	29.93	
	McBain[15]	Stim	15	0.213	−0.507 to 0.933	39.82	
	McLachlan[10]	Stim	12	0.491	−0.335 to 1.317	30.26	
I-V pooled SMD ($I^2=0.00$, df=2, $P=0.593$)				0.469	0.014 to 0.923		0.043
	Cheng[14]	Control	13	0.05	−0.719 to 0.819		0.899
V_C (l)	Cheng[14]	Stim	13	0.786	−0.045 to 1.616	45.19	
	McBain[15]	Stim	15	0.642	−0.112 to 1.396	54.81	
I-V pooled SMD ($I^2=0.00$, df=1, $P=0.802$)							0.013
	Cheng[14]	Control	13	0.12	−0.650 to 0.890		0.760
FEV_1 (l)	Cheng[14]	Stim	13	0.314	−0.465 to 1.093	32.46	
	McBain[15]	Stim	15	0.258	−0.464 to 0.981	37.78	
	McLachlan[10]	Stim	12	0.35	−0.463 to 1.163	29.77	
I-V pooled SMD ($I^2=0.00$, df=1, $P=0.986$)				0.304	−0.140 to 0.748		0.180
	Cheng[14]	Control	13	0	−0.769 to 0.769		1.000
PEF ($l\ s^{-1}$)	Cheng[14]	Stim	13	1.078	0.196 to 1.959	27.41	
	McBain[15]	Cough	15	0.431	−0.302 to 1.165	39.61	
	McLachlan[10]	Stim	12	0.18	−0.624 to 0.983	32.98	
I-V pooled SMD ($I^2=12.4$, df=2, $P=0.319$)				0.526	−0.064 to 1.987		0.026
	Cheng[14]	Control	13	−0.014	−0.783 to 0.754		0.971
MEP (cmH_2O)	Cheng[14]	Stim	13	0.968	0.107 to 1.828	46.36	
	McLachlan[10]	Stim	12	0	−0.800 to 0.800	53.64	
D-L pooled SMD ($I^2=61.6$, df=1, $P=0.107$)				0.47	−0.478 to 1.418		0.134
	Cheng[14]	Control	13	0.262	−0.514 to 1.038		0.508

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