Effectiveness of transcranial direct current stimulation preceding cognitive behavioural management for chronic low back pain: sham controlled double blinded randomised controlled trial

Kerstin Luedtke,[1] Alison Rushton,[2] Christine Wright,[2] Tim Jürgens,[1] Astrid Polzer,[1] Gerd Mueller,[3] Arne May[1]

EDITORIAL by O'Connell and Wand

[1]Department of Systems Neuroscience, University Medical Centre Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany
[2]School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK
[3]Backpain Clinic "Am Michel", Ludwig-Erhard-Strasse 18, 20459 Hamburg, Germany
Correspondence to: A May
a.may@uke.de

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STUDY QUESTION

Does transcranial direct current stimulation (tDCS) reduce pain and disability in patients with non-specific chronic low back pain and, when applied before a cognitive behavioural group programme, does it influence the outcome of the programme?

SUMMARY ANSWER

Transcranial direct current stimulation does not influence pain or disability in patients with non-specific chronic low back pain nor does it influence the outcomes of a cognitive behavioural group programme when applied immediately before the programme.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Numerous small trials have suggested that transcranial direct current stimulation can reduce chronic pain, but there have been no adequately powered randomised controlled trials. Systematic reviews and meta-analyses indicated a small beneficial effect but also highlighted the high risk of bias of existing trials. This new study suggests that transcranial direct current stimulation over the motor cortex has no overall benefit for the reduction of pain and disability in patients with non-specific chronic low back pain. Furthermore, when it was applied immediately before a cognitive behavioural group intervention it did not influence the outcome of the intervention.

Design

A double blind parallel group randomised controlled trial with a six month follow-up was conducted between February 2011 and March 2013 at an interdisciplinary chronic pain centre in Hamburg, Germany. Patients were randomised to receive either active (anodal stimulation of the motor cortex at 2 mA for 20 minutes) or sham stimulation (identical electrode position, stimulator switched off after 30 seconds) for five consecutive days immediately before a cognitive behavioural management programme. Computer generated randomisation lists for active or sham stimulation with permuted blocks of 20 allowed for equal numbers in each study arm at various time points. Allocation concealment was achieved by individual five digit stimulation codes pre-programmed to set off active or sham stimulation. The stimulation codes also served to allow participant and physiotherapist blinding. Assessor and data analyses were blinded by coding the active and the sham group as A and B by an independent researcher.

Participants and setting

We recruited 135 patients who had had chronic non-specific low back pain for more than 12 weeks (as classified by European guidelines).

Primary outcomes

Two primary outcome measures were pain intensity (0-100 visual analogue scale) and disability (Oswestry disability index). The primary endpoints were assessed after stimulation and after cognitive behavioural management.

Main results and the role of chance

Analyses of covariance with baseline values as covariates indicated that tDCS was ineffective for the reduction of pain (1 mm difference (99% confidence interval −8.69 to 6.3, P=0.68) between groups) and disability (0 points difference (−1.73 to 1.98, P=0.86) between groups) and did not influence the outcome of cognitive behavioural management (2 mm difference on visual analogue scale (−10.32 to 6.73, P=0.58) between groups; 1 point difference on Oswestry disability index (−2.45 to 2.62, P=0.92) between groups).

Harms

tDCS was well tolerated with frequent but transitory and mild side effects.

Bias, confounding, and other reasons for caution

Bias was judged to be low. The trial methods and technical equipment allowed successful blinding of patients and investigators throughout the trial. Based on a valid sample size calculation, we included a sufficient number of participants to show an effect on pain and disability.

Generalisability to other populations

Results should apply to other populations with chronic low back pain defined according to the European guidelines for chronic low back pain.

Study funding/potential competing interests

This study was funded by DFG (MA 1862/10-1) and NeuroImageNord.

Trial registration number

Current controlled trials ISRCTN89874874.

Mean (SD) values and results from analysis of covariance (ANCOVA) for visual analogue scale (VAS) for pain and Oswestry disability index (ODI) after stimulation and after cognitive behavioural management with 99% confidence intervals for differences between groups

	After stimulation				After CBT			
Outcome measure	Mean (SD) anodal	Mean (SD) sham	Mean difference between groups (99% CI)	P value	Mean (SD) anodal	Mean (SD) sham	Mean difference between groups (99% CI)	P value
VAS (mm)	42 (24), n=60	41 (23), n=62	1 (−8.69 to 6.3)	0.68	26 (23), n=60	23 (18), n=58	3 (−10.32 to 6.73)	0.58
ODI (points)	15 (7), n=61	14 (6), n=61	1 (−1.73 to 1.98)	0.86	7 (6), n=53	7 (5), n=54	0 (−2.45 to 2.62)	0.92

CBT = cognitive behavioural management

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Time to benefit for colorectal cancer screening: survival meta-analysis of flexible sigmoidoscopy trials

Victoria Tang,[1] W John Boscardin,[1 2] Irena Stijacic-Cenzer,[1 2] Sei J Lee[1 2]

EDITORIAL by Brenner

[1]San Francisco VA Medical Center, San Francisco, CA 94121, USA
[2]Division of Geriatrics, University of California San Francisco CA, USA
Correspondence to: V Tang
Victoria.Tang@ucsf.edu

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STUDY QUESTION

What is the timing to survival benefit being seen after a screening flexible sigmoidoscopy?

SUMMARY ANSWER

For every 1000 people screened with flexible sigmoidoscopy it would take approximately 10 years for one colorectal cancer related death to be prevented.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Guidelines recommend targeting cancer screening to older adults (50-74 years) whose life expectancy exceeds the time to benefit for screening. We found that it would take 9.4 years for one colorectal cancer related death to be prevented for every 1000 people screened, suggesting that flexible sigmoidoscopy screening should be targeted toward patients with a life expectancy of greater than 10 years.

Selection criteria for studies

We focused on randomised controlled trials comparing screening flexible sigmoidoscopy with no screening identified by the 2013 Cochrane Collaboration systematic review entitled "Flexible sigmoidoscopy versus faecal occult blood testing for colorectal cancer screening in asymptomatic individuals," Medline, and Cochrane Library databases. We excluded trials with fewer than 100 flexible sigmoidoscopy screenings. A survival meta-analysis was performed of the identified trials.

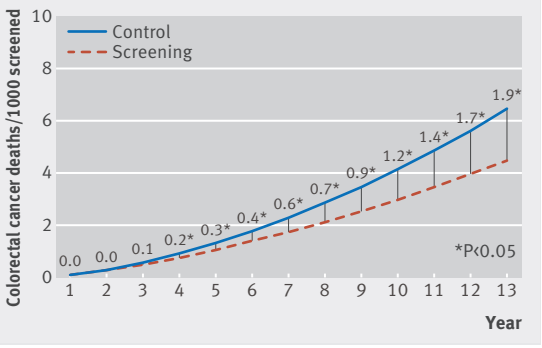
Primary outcome

Our main outcome measure was time to survival benefit of colorectal cancer screening with flexible sigmoidoscopy.

Main results and role of chance

This meta-analysis found that for every 5000 people screened with flexible sigmoidoscopy it would take 4.3 years (95% confidence interval 2.8 to 5.8) to prevent one colorectal cancer related death (absolute risk reduction 0.0002). For every 2000 people screened with flexible sigmoidoscopy it would take 6.6 years (95% confidence interval 5.1 to 5.8) to prevent one colorectal cancer related death (absolute risk reduction 0.0002), and for every 1000 people screened it would take 9.4 years (7.6 to 11.3) to prevent one colorectal cancer related death (absolute risk reduction 0.001).

Pooled mortality curves for colorectal cancer



Bias, confounding, and other reasons for caution

There is uncertainty around the rates of serious complications from screening flexible sigmoidoscopy, and so it is unclear what level of delayed benefit would justify exposing patients to immediate harms. The results of meta-analysis combining a small number of studies may be sensitive to the choice of meta-analytical methods; however, our results were consistent across both fixed and random effects meta-analysis. Also, our analysis was limited to mortality benefit of flexible sigmoidoscopy screening and may underestimate the time to benefit to avoid symptoms from cancer.

Study funding/potential competing interests

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Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: meta-analysis of individual participant data from prospective cohort studies of the CHANCES consortium

Ute Mons on behalf of the CHANCES consortium*

Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ), Heidelberg, Germany

Correspondence to: Ute Mons
u.mons@dkfz.de

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STUDY QUESTION

What is the impact of smoking and smoking cessation on cardiovascular events and mortality among older adults?

SUMMARY ANSWER

Also among older adults smoking strongly contributes to acute coronary events, strokes, and cardiovascular deaths, and advances cardiovascular mortality by more than five years. At the same time, quitting smoking is still beneficial in reducing the excess risk caused by smoking.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Even though most cardiovascular events occur in older adults, this age group has been understudied when it comes to the impact of smoking and the benefits of smoking cessation on cardiovascular health. Using data from a large consortium of cohorts, we demonstrate that smoking is a strong independent risk factor for cardiovascular events and mortality among older adults and that smoking cessation is still beneficial in reducing the cardiovascular excess risk caused by smoking.

Participants and setting

We used data from 503 905 participants aged 60 and older from 25 cohorts of the CHANCES consortium.

Design, size, and duration

Individual participant data from 25 prospective cohort studies were harmonised, analysed separately employing Cox proportional hazard regression models, and combined by meta-analysis. We report hazard ratios and risk advancement/reversion in years. Overall, 503 905 participants aged 60 and over were included in this study, and the mean follow-up time was between 8 and 13 years for most of the studies.

Impact of smoking and smoking cessation on cardiovascular mortality, hazard ratios, and risk advancement or reversion in years

	Hazard ratio (95% CI)	Risk advancement/ reversion in years (95% CI)
Former and current smokers *v* never smokers		
Never smokers	1 (ref)	0 (ref)
Former smokers	2.07 (1.82 to 2.36)	5.50 (4.25 to 6.75)
Current smokers	1.37 (1.25 to 1.49)	2.16 (1.38 to 2.93)
Former smokers by time since smoking cessation *v* current smokers		
Current smokers	1 (ref)	0 (ref)
Quit ≤5 years ago	0.90 (0.81 to 1.00)	−0.82 (−1.72 to 0.07)
Quit 5-9 years ago	0.84 (0.73 to 0.95)	−1.34 (−2.29 to −0.39)
Quit 10-19 years ago	0.78 (0.71 to 0.85)	−1.96 (−2.69 to −1.24)
Quit ≥20 years ago	0.61 (0.54 to 0.69)	−3.94 (−4.86 to −3.03)

Main results and the role of chance

Overall, 37 952 participants died from cardiovascular disease. Smokers had twice as much risk of cardiovascular mortality compared with individuals who had never smoked (hazard ratio 2.07, 95 % CI 1.82 to 2.36); the risk of dying from cardiovascular disease was advanced in smokers by 5.5 years. The risk of experiencing acute coronary events for smokers was also roughly twice as big (hazard ratio 1.98 (1.75 to 2.25)), and 1.6 times greater in the case of strokes (hazard ratio 1.58 (1.40 to 1.78)). The excess risk from smoking increased with higher levels of cigarette consumption, while the increased excess risk among former smokers dropped with time after smoking cessation in a dose-response manner. Relative risk estimates for acute coronary events and for stroke events were somewhat lower than for cardiovascular mortality, but patterns were similar .

Bias, confounding, and other reasons for caution

The true associations of smoking and smoking cessation with cardiovascular outcomes are probably stronger than were observed in our study because we included only participants aged 60 and older (heavier and long term smokers might be under-represented owing to their increased mortality risks), because smoking behaviour was self reported (social desirability or imperfect recall could have led to under-reporting of smoking and misclassification of smokers), and because smoking was assessed at baseline only (smoking cessation in baseline smokers and relapses in former smokers over follow-up are not taken into account).

Generalisability to other populations

We included a large number of cohorts from Europe (covering eastern, northern, southern, western, and central Europe) and the United States, and by covering such a wide geographical area, our results are broadly generalisable to older populations from western industrialised countries.

Study funding/potential competing interests

Data used throughout this study are derived from the CHANCES project. The project received funding by the FP7 framework programme of DG-RESEARCH in the European Commission (grant agreement no. HEALTH-F3-2010-242244).