Ergogenic and Physiologic Effects of tDCS on Maximal Aerobic Performance: Protocol Description

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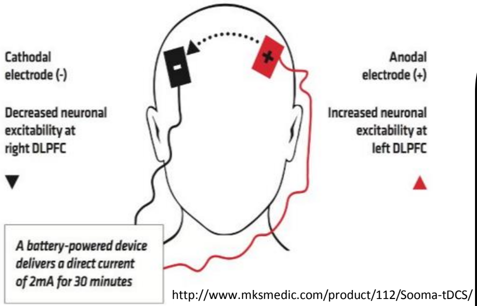
BACKGROUND



http://www.mksmedic.com/product/112/Sooma-tDCS/

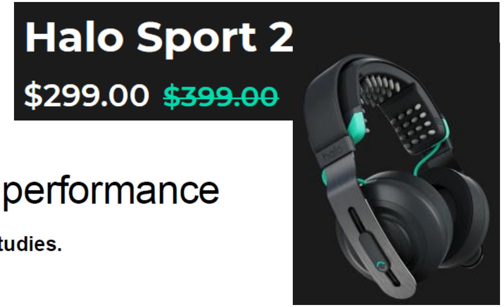
- Transcranial direct current stimulation (tDCS) = **neuromodulation method** *transiently* improving functions of stimulated area
- Can improve strength (isometric) and performance (cycling)[1]
- No study controlled for physiological variables
- What about runners?
- Increasing media attention

frontiers in Physiology

"Brain-Doping," Is It a Real Threat?

Darías Holgado [1,2]*, Miguel A. Vadillo [3] and Daniel Sanabria [2]*

[1] Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada, Spain, [2] Department of Experimental Psychology, Mind, Brain and Behavior Research Centre, University of Granada, Granada, Spain, [3] Department of Basic Psychology, Autonomous University of Madrid, Madrid, Spain



NATURE | NEWS

'Brain doping' may improve athletes' performance

Electrical stimulation seems to boost endurance in preliminary studies.

Sara Reardon

[1] Machado et al, *Brain Stim*, 2018

OBJECTIVES

AIM – Randomized Controlled Trial

Investigate effects of bilateral motor cortex (M1) single tDCS session on performance (i.e., time to exhaustion – **TTE**) and on performance-related physiological parameters (i.e., aerobic profile) during a maximal treadmill test

RESEARCH QUESTIONS

1

Does active M1 tDCS significantly increases **TTE** as compared to sham ?

Primary Outcome

2

Does active M1 tDCS significantly decreases **ratings of perceived exertion** (RPE) as compared to sham ?

Secondary Outcome

3

Difference (active/sham) on **physiological parameters** (VO2max, RER, lactatemia, HR) ?

Secondary Outcome

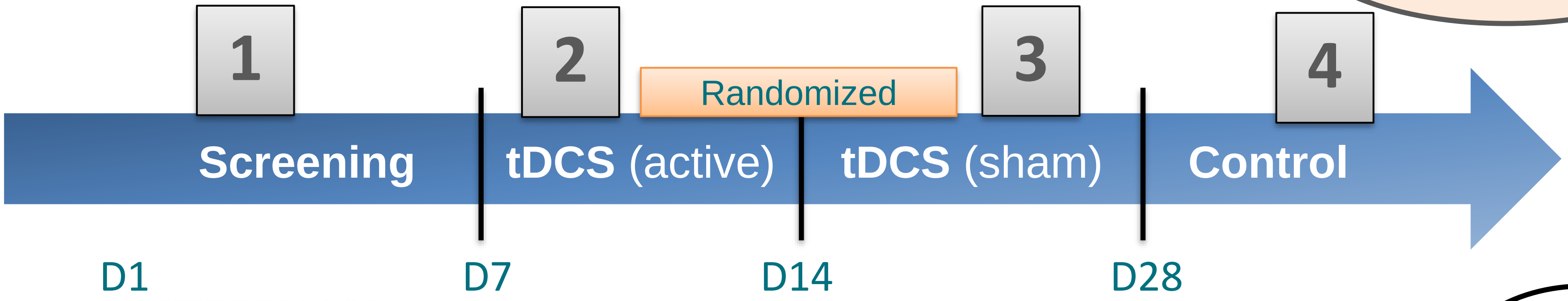
4

Influence of **baseline athletic level** (VO2max) on tDCS response ?

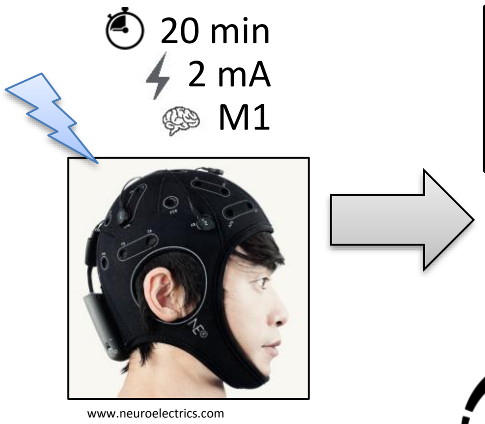
Secondary Outcome

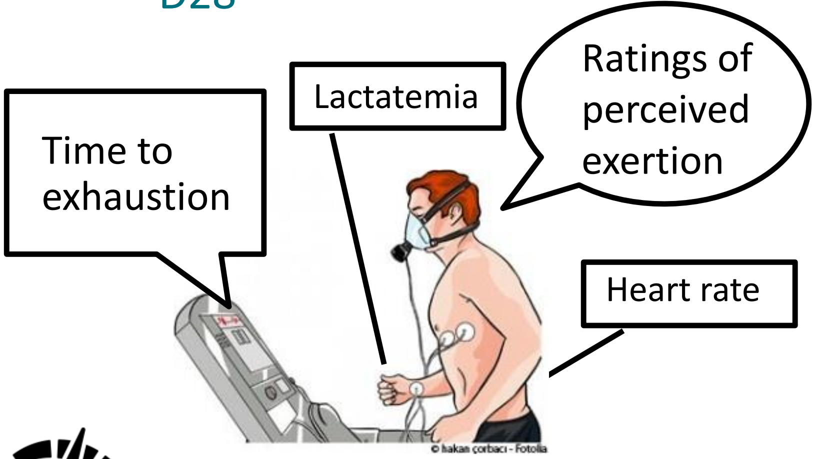
METHODS

Status: 3/25 subjects completed



- Informed consent
- Life hygiene & training habits
- tDCS safety screening **[2]**
- Inclusion/exclusion criteria
- **Incremental exhaustive test**



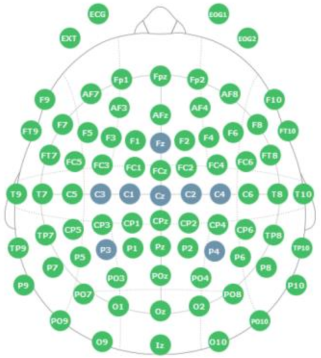


90% max. aerobic speed

[2] Bornheim et al, *Am J Phys Med Rehabil*, 2019

IMPACT

- First RCT performed on **large sample**
- First tDCS montage **optimized** to target the motor network [3]
- tDCS effects on **physiological variables**
- Build **tDCS-responder** phenotype (baseline VO2max, lactatemia curves…)?
- Provide **robust data** to legislating institutions (doping)

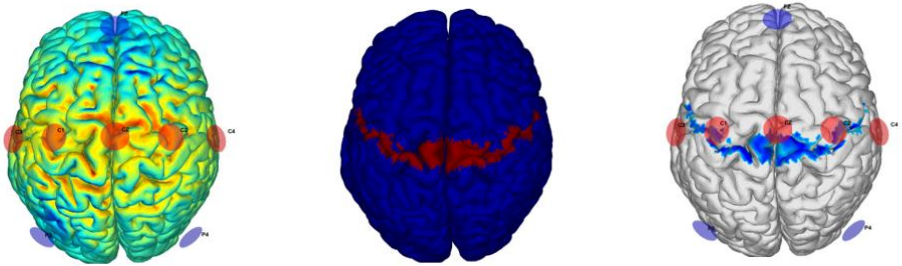


Neuroelectrics Stimweaver

Alex Hutchinson

[3] Ruffini et al, *Neuroimage*, 2014

Thank you!



Clinicaltrials.gov n° NCT04005846

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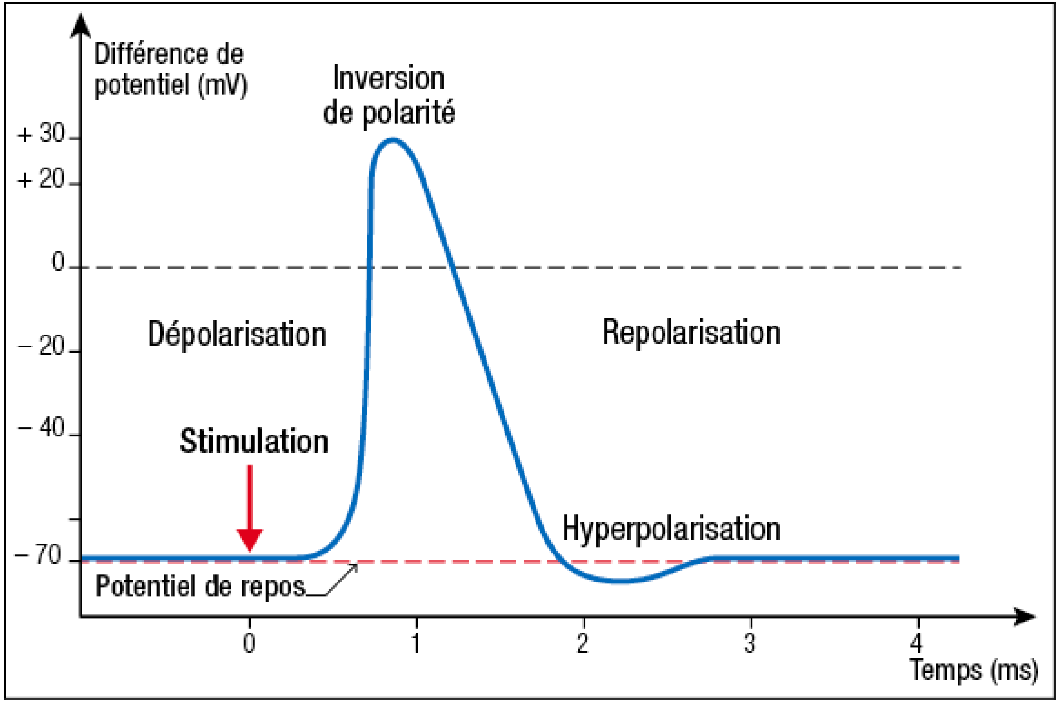
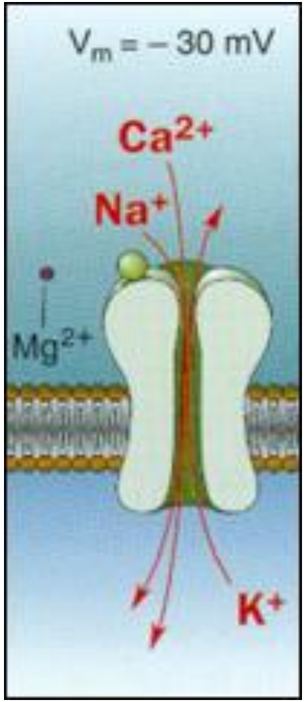
Back up slides

tDCS mechanisms of action

Short term effects



Long term



Effect of transcranial direct current stimulation on exercise performance: A systematic review and meta-analysis

Daniel G. da S. Machado [a], Gozde Unal [b], Suellen M. Andrade [c], Alexandre Moreira [d], Leandro R. Altimari [a], André R. Brunoni [e], Stéphane Perrey [f], Alexis R. Mauger [g], Marom Bikson [b], Alexandre H. Okano [a, h, *]

Table 1
Characteristics of the included studies.

Study information					Sample		tDCS set-up			
Authors	Design	Exp	Exercise type	Exercise Protocol	n (M/W)	Training status	Anode or cathode Return electrode	Intensity (mA)	Density (mA/cm^2)	Duration (Min)
Abdelmoula et al. [41]	Cross	1	Isometric strength	35% of MIVC of elbow flexion	11 (8 M/3 W)	N/D	Left M1 Right shoulder	1.5	0.043	10
Cogiamanian et al. [40]	Parallel	1	Isometric strength	35% of MIVC of elbow flexion	24 (10 M/14 W)	N/D	***A*** Right M1 Right shoulder	1.5	0.043	10
	Parallel	2	Isometric strength	35% of MIVC of elbow flexion	24 (10 M/14 W)	N/D	***C*** Right M1 Right shoulder	1.5	0.043	10
Kan et al. [45]	Cross	1	Isometric strength	30% of MIVC of elbow flexion	15 (M)	N/D	Right M1/Right shoulder	2.0	0.083	10
Muthalib et al. [46]	Cross	1	Isometric strength	30% of MIVC of elbow flexion	15 (M)	N/D	Right M1/Right shoulder	2.0	0.083	10
Radel et al. [80][a]	Cross	1	Isometric strength	35% of MIVC of elbow flexion	22 (13 M/9 W)	N/D	***A*** C2 and ***C*** 4 cm around (HD-tDCS 4x1)	2.0	N/D	N/D
	Cross	2	Isometric strength	35% of MIVC of elbow flexion	22 (13 M/9 W)	N/D	HD-tDCS (***A***) AF4 and (***C***) 4 cm around	2.0	N/D	N/D
Williams et al. [100][a]	Cross	1	Isometric strength	20% of MIVC of elbow flexion	18 (9 M/9 W)	9 active/9 low active	Right M1 Fp2	1.5	0.043	≤20
Angius et al. [90]	Cross	1	Isometric strength	20% MIVC of knee extension	9 M	Recreationally active	***A*** Left M1/Fp2	2.0	0.17	10
	Cross	2	Isometric strength	20% MIVC of knee extension	9 M	Recreationally active	***A*** Left M1 Shoulder	2.0	0.17	10
Flood et al. [81]	Cross	1	Isometric strength	30% MIVC of knee extension	12 (M)	Recreationally active	C3/C4 and 5 cm around (HD-tDCS 4X1)	2.0	0.057	20
Hazime et al. [61]	Cross	1	MIVC	Shoulder internal/external rotators	8 (W)	Handball athletes	C3/C4 Fp2/Fp1	2.0	0.057	20
Frazer et al. [62][b]	Cross	1	MIVC	Wrist flexors	14 (6 M/8 W)	N/D	Left C3 Fp2	2.0	0.08	20
Maeda et al. [58][a]	Parallel	1	Isokinetic strength	5 reps of eccentric knee extension/flexion	24 (12 M/12 W)	N/D	M1 Shoulder	2.0	0.08	10
Montenegro et al. [63]	Cross	1	Isokinetic strength	10 reps of knee extension/flexion	14 (M)	Trained in RT (≥6 months)	Left M1 Fp2	2.0	0.057	20
Sales et al. [64]	Cross	1	Isokinetic strength	5 reps of knee extension	19 (M)	Physically active	T3 Fp2	2.0	0.057	20
Hendy et al. [66][a]	Cross	1	Dynamic strength	1RM wrist extension	10 (5 M/5 W)	N/D	Right M1 Fp1	2.0	0.08	20
Lattari et al. [65]	Cross	1	Dynamic strength	10RM elbow flexion	10 (M)	Trained in RT (≥6 months)	F3 Fp2	2.0	0.057	20
Angius et al. [43]	Cross	1	Cycling	TTE at 70% PP	12 (8 M/4 W)	Recreationally active	***A*** both M1/shoulders	2.0	0.057	10
	Cross	2	Cycling	TTE at 70% PP	12 (8 M/4 W)	Recreationally active	***C*** both M1/shoulders	2.0	0.057	10
Angius et al. [47]	Cross	1	Cycling	TTE at 70% PP	9 (M)	Recreationally active	Right M1/F4	2.0	0.17	10
Barwood et al. [44]	Cross	1	Cycling	20 km time trial	6 (M)	Physically active	T3/Fp2	1.5	0.43	20
	Cross	2	Cycling	TTE at 75% PP	8 (M)	Physically active	T3/Fp2	2.0	0.44	20
Lattari et al. [59]	Cross	1	Cycling	TTE at 100% PP	11 (W)	Moderately active	F3/Fp2	2.0	0.057	20
Okano et al. [35]	Cross	1	Cycling	Incremental maximum	10 (M)	Athletes (cyclists)	T3/Fp2	2.0	0.057	20
Sasada et al. [60]	Cross	1	Cycling	Wingate test	23 (17 M/6 W)	Athletes (various)	Cz/Fp2	2.0	0.057	15
Vitor-Costa et al. [42]	Cross	1	Cycling	TTE at 80% PP	11 (M)	Physically active	***A*** both M1/Inion	2.0	0.056	13
	Cross	2	Cycling	TTE at 80% PP	11 (M)	Physically active	***C*** both M1/Inion	2.0	0.056	13

Note: [a] = tDCS applied during exercise; [b] = multiple tDCS sessions; A/C = anode/cathode electrode; Cross = crossover design; Exp = experiment; HD-tDCS = high-definition transcranial direct current stimulation; M/W = men/women; M1 = primary motor cortex; MIVC = maximal isometric voluntary contraction; N/D = not described; PP = peak power; RM = repetition maximum; RT = resistance training; tDCS = transcranial direct current stimulation; TTE = time to exhaustion.

A

Study or Subgroup	Anodal Mean [s]	Anodal SD [s]	Anodal Total	Placebo Mean [s]	Placebo SD [s]	Placebo Total	Weight	Mean Difference IV, Random, 95% CI [s]
Angius et al. 2015	994.8	509.4	9	880.8	517.2	9	1.9%	114.00 [-360.27, 588.27]
Angius et al. 2018	795	260.4	12	645.6	181.8	12	13.5%	149.40 [-30.29, 329.09]
Vitor-Costa et al. 2015	491	100	11	407	69	11	84.6%	84.00 [12.20, 155.80]
Total (95% CI)			**32**			**32**	**100.0%**	**93.41 [27.39, 159.43]**

Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 2 (P = 0.80); I² = 0%
Test for overall effect: Z = 2.77 (P = 0.006)

B

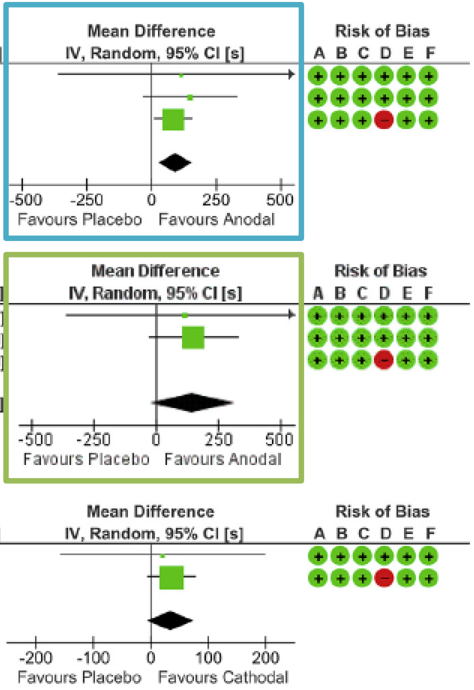
Study or Subgroup	Anodal Mean [s]	Anodal SD [s]	Anodal Total	Placebo Mean [s]	Placebo SD [s]	Placebo Total	Weight	Mean Difference IV, Random, 95% CI [s]
Angius et al. 2015	994.8	509.4	9	880.8	517.2	9	12.6%	114.00 [-360.27, 588.27]
Angius et al. 2018	795	260.4	12	645.6	181.8	12	87.4%	149.40 [-30.29, 329.09]
Vitor-Costa et al. 2015	491	100	11	407	69	11	0.0%	84.00 [12.20, 155.80]
Total (95% CI)			**21**			**21**	**100.0%**	**144.96 [-23.07, 312.99]**

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 1.69 (P = 0.09)

C

Study or Subgroup	Cathodal Mean [s]	Cathodal SD [s]	Cathodal Total	Placebo Mean [s]	Placebo SD [s]	Placebo Total	Weight	Mean Difference IV, Random, 95% CI [s]
Angius et al. 2018	666	256.8	12	645.6	181.8	12	5.1%	20.40 [-157.62, 198.42]
Vitor-Costa et al. 2015	443	11	11	407	69	11	94.9%	36.00 [-5.29, 77.29]
Total (95% CI)			**23**			**23**	**100.0%**	**35.20 [-5.02, 75.43]**

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%
Test for overall effect: Z = 1.72 (P = 0.09)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)

Fig. 3. Forest plot showing mean difference from the comparison between anodal vs. sham (A) and cathodal vs. sham (C) transcranial direct current stimulation applied before exercise in terms of time to exhaustion in whole-body cycling exercise. Note: given that the result of the anodal vs. sham analysis shown in panel A was driven by one single study (Vitor-Costa et al., 2015), it was removed from the analysis and the results were not significant (panel B). Risk of bias was deemed as "low risk of bias" ("+"), "high risk of bias" ("-") or "unclear risk of bias" ("?")

Eligibility Criteria

- Inclusion :

- [ ] Adulte (18-35 ans)
- [ ] Sexe masculin

Durée d'entraînement hebdomadaire

  - [ ] comprise entre 2 et 4 heures (**groupe débutant**) OU
  - [ ] supérieure à 4 heures (**groupe confirmé**)

- Exclusion :

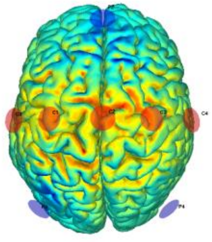
- [ ] Ne fume PAS
- [ ] Ne restreint PAS son régime alimentaire (sauf allergies ou régime végétarien)
- [ ] ABSENCE de lésion/douleur/gêne au niveau des membres inférieurs au cours des 6 dernières semaines
- [ ] Ne prend PAS de compléments alimentaires quotidiens
- [ ] Ne consomme PAS d'alcool à raison de plus de 4 unités par semaine
- [ ] Ne consomme PAS de caféine à raison de plus de 10 unités par semaine
- [ ] Ne suit PAS un traitement médicamenteux impactant le système nerveux central
- [ ] N'obtient AUCUN « Oui » à la partie 'Risque élevé' du TSST
- [ ] N'obtient PAS plus d'un « Oui » à la partie 'Risque relatif' du TSST

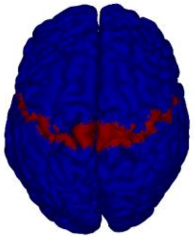
Methods

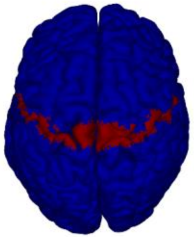
- **Eligibility Questionnaire**: training habits, previous injuries/pain, smoking – drinking – coffee consumption habits, dietary supplementation, medication
- tDCS Safety Screening Tool (**TSST**)
- **tDCS** applied by a blind investigator right before test to exhaustion (20’ – 2 mA)
- **Incremental test to exhaustion**: warm-up 5’ – 8 km/h, increments of 2 km/h every 3’ up to 16 km/h, then 1 km/h every 3’ until exhaustion. Lactatemia & Borg RPE scale at the end of each increment
- **Time to exhaustion trial**: warm-up 5’ – 8 km/h then 90% MAS until exhaustion. Lactatemia & Borg RPE scale every 5’
- Active/sham & adverse effect questionnaires

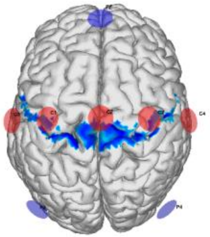
tDCS montage

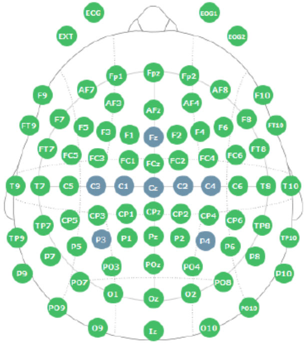
Optimized to target the motor network with the highest current density (8 electrodes – 4 mA total – max. 2 mA/electrode)











Statistical Analyses

- Sample size estimation: **25 – 30** subjects per group
- For the variables TTE (primary), RPE, VO2max, MAS, LT, RER, max HR (secondary): check for significant difference in active vs. sham using **Student' t test** (if normality OK) or **Wilcoxon-Mann-Whtiney** (if normality KO)
- For influence of baseline physical fitness: compare **delta TTE/RPE** between the 2 groups (recreationally vs. active)
- Exploratory: differences in **HR** pre-post tDCS & active vs sham
- Interim analysis at n=25 in each group

Table 2. Nombre de sujets **par groupe** en fonction de la puissance et de « l'effect size »

	Puissance	
	80%	90%
« Effect size »	n	n
0.1	1571	2103
0.2 (small effect)	394	527
0.3	176	235
0.5 (moderate effect)	64	86
0.7	34	44
0.8 (large effect)	**26**	**34**
0.85	**23**	**31**
0.90	**21**	**27**
0.95	**19**	**25**
1	**17**	**23**
1.5	**9**	**11**