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## Introduction

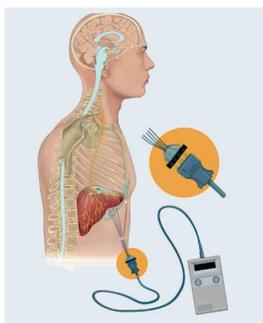
Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder typically leading to death because of respiratory failure. In healthy subjects, a single session of cathodal tsDCS applied over C3-C5 spinal segments induces persistent potentiation in the respiratory control system (Niérat et al., 2014).

## Aim

We evaluated whether cathodal tsDCS could modulate intradiaphragmatic EMG in ALS patients implanted with diaphragm pacing.

## Methods

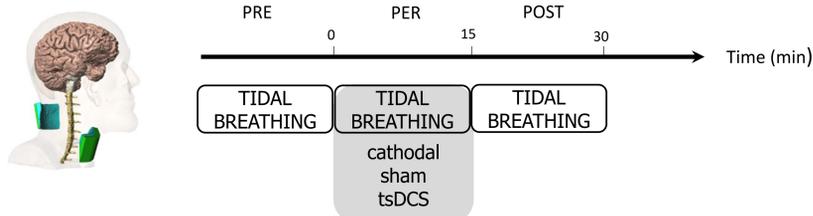
This study is ancillary to a randomized, triple blinded, controlled interventional trial of a laparoscopically implanted diaphragm pacing device (NeuRx Diaphragm Pacing System (DPS) TM, Synapse, Oberlin, Ohio, USA) in 74 patients with ALS, conducted in France (NCT01583088). This trial was designed to assess the impact of the DPS on the decline of forced vital capacity (FVC).



Nine ALS patients (3 females, without indication of non-invasive ventilation) received in a randomized, cross-over, double-blinded fashion a single session (15min) of cathodal or sham tsDCS in two different visits.

Variable	Data
Gender ratio M/F	2/1
Age (years) (med [min-max])	54 [26-61]
Site of onset (ratio spinal / bulbar)	3.5/1
ALSFRS-R score (med [min-max])	33 [23-38]
Height (cm) (med [min-max])	171 [158-180]
BMI (kg/m <sup>2</sup> ) (med [IQR])	22.8 [22-31.2]
FVC (%predicted) (med [IQR])	80 [68-89]

For tsDCS, one electrode was placed on the midline of the posterior part of the neck to cover cervical spinal segments C3-C5, and the other electrode was placed just below the cervicomental angle (Niérat et al., 2014). Polarity of stimulation refers to the spinal electrode. The stimulus intensity was set at 2.5mA and was applied over a 15-min period (Cogiamanian et al., 2008; Winkler et al., 2010; Lamy et al., 2012) resulting in a current density of 0.071 mA/cm<sup>2</sup> and a delivered total charge of 64mC/cm<sup>2</sup>.



Diaphragm electrodes were connected to an EMG recording system allowing to record bilateral intradiaphragmatic EMG bursts during spontaneous ventilation.

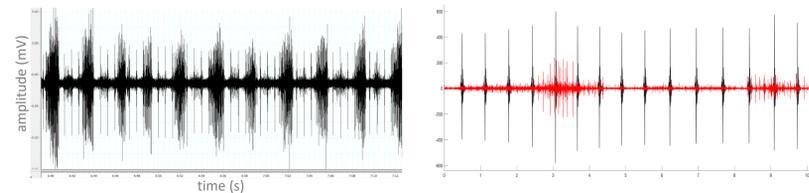
Diaphragm weakness was assessed bilaterally by the latency of motor responses following phrenic nerves stimulation.

Recordings were made during three epochs of 15min each: before (PRE), during stimulation (PER) and immediately after current offset (POST). ECG artefacts were removed from the signal and RMS of EMG bursts were averaged across trials for each 15min epoch according to the side of diaphragmatic weakness.

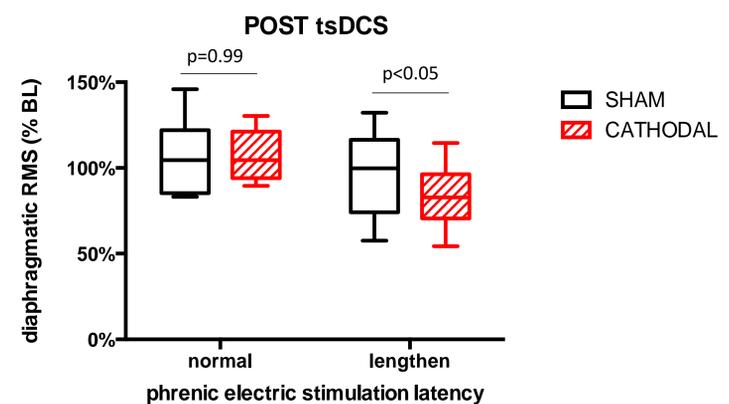
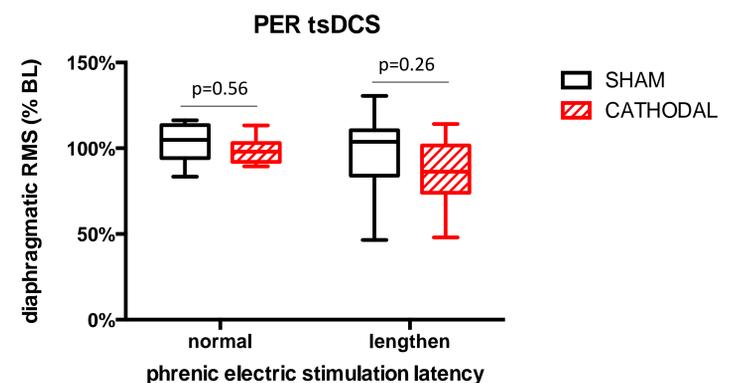
Wilcoxon tests were used for statistical analyses

## Results

To analyse EMG burst, electrocardiogram (ECG) contaminations had been removed from EMG signal. To that end, the ECG was first roughly reconstructed using the EMG spectrum below 30Hz, enabling to locate the QRS complexes. Then, a typical EMG pattern around the QRS was obtained using a mean of the EMG signal on 168ms-wide windows. Finally, this typical EMG pattern was subtracted from all the QRS windows.



Example of raw intradiaphragmatic EMG (black trace) and intradiaphragmatic EMG after ECG extraction (red trace).



## Conclusion

Contrary to our expectations, this study shows that cathodal tsDCS does not induce increase in intradiaphragmatic EMG activity and is not suitable as a potential treatment for hypoventilation in ALS patient. Furthermore, our results show that tsDCS failed to modulate RMS on the less affected side and provide direct evidence for a deleterious effect of cathodal tsDCS on the most affected side of diaphragm in ALS patients. tsDCS-induced excitotoxicity on phrenic motoneurons (especially on slow motor units) is likely involved.

## References

- Cogiamanian et al., Clin Neurophysiol 2008; 119:2636-2640
- Lamy et al., J Neurophysiol 2012; 108:906-914
- Niérat et al., J Neurosci 2014; 34: 14420 –14429
- Winkler et al., Clin Neurophysiol 2010; 121:957-961

## Acknowledgement

This work was supported by a "Legs Poix" grant from the "Chancellerie de l'Université de Paris", Paris, France; a support grant from "Association pour le Développement et l'Organisation de la Recherche en Pneumologie et sur le Sommeil", Paris, France; and by the French Government (IHU-A-ICM) "Investissement d'avenir" ANR-10-IAIHU-06 program.