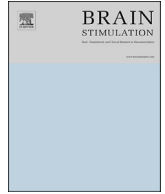




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## Effects of COVID-19 lockdown on chronic drug-resistant pain patients treated using brain stimulation approaches



### Keywords:

Transcranial direct current stimulation  
Motor cortex  
Pain  
COVID-19  
Lockdown

Chronic pain often shows insufficient response to pharmacological treatments. Non-invasive brain stimulation (NIBS) of the motor cortex has been proposed as an alternative therapeutic approach [1,2]. This therapeutic intervention requires repeated NIBS sessions once-daily for 1 or 2 weeks followed by a maintenance protocol [2–4]. In our hospital, we usually apply ten NIBS daily sessions (two weeks, Monday to Friday); we will refer to this period as induction phase. After the induction phase, responsive subjects enter into the maintenance phase. Maintenance phase consists of one NIBS session every two weeks (for some patients this interval is shortened to 7–10 days). We used both repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS). In our lab, pain relief is similarly obtained with the two techniques. Currently, approx. 90% of our patients are receiving tDCS. A very small number of patients receiving tDCS are treated at home. In these cases, the caregiver is trained to apply the tDCS and we follow the patients remotely. Mid of March 2020, 74 patients were included in the maintenance phase of tDCS treatment at the Hospital and 7 patients were in the same phase but at home. Due to COVID-19 pandemic lockdown, we were not allowed to receive the patients at the Hospital to minimize the risk of contagion. Here, we present and analyse the effects of one-month lockdown on these patients and the estimated cost of starting again in the next future. We telephonically interviewed both the patients that habitually received tDCS at the Hospital (so that were forced to discontinue the treatment) and the patients that were receiving tDCS at home before the lockdown (they did not discontinue the treatment). During the phone interview, we asked to quantify the pain they have on a numeric rating scale (NRS) from 0 to 10, so we have the possibility to compare it with the pain rating of the last tDCS session they received (we use to collect this info at every hospital visit or at home NIBS session). We observed pain worsening of patients that discontinued the treatment ( $N = 74$ ; female = 49; mean age  $52.3 \pm 12.0$ ; NRS: last evaluation before lockdown  $5.0 \pm 2.4$  and after  $6.7 \pm 1.7$ , paired  $t$ -test,  $p < 0.0001$ ), but not of patients that did not ( $N = 7$ ; female = 4; mean age

$42.3 \pm 13.5$ ; NRS: before lockdown  $5.6 \pm 2.6$  and after  $5.6 \pm 2.4$ , paired  $t$ -test,  $p = 0.992$ ). These data suggest that the subjects who discontinued the maintenance sessions are losing the pain relief effects, probably with effects on their quality of life. Moreover, these effects do not depend on the lockdown per se since the other group is maintaining the analgesic effects. Probably, most of the patients that discontinued the treatment will require a new induction phase. As reported before, the induction period consists of 10 sessions, so estimating that approx. 90% of patients will require a new induction, when we will be allowed to restart we will have to programme about 650 tDCS sessions, which are approx. 520 more than the planned sessions (the planned sessions were 2 per month). This will cost approx. €52,000 (considering €100 per tDCS session). Approximately 80% of patients we attend live at less than 50 Km from the Hospital so they use to travel from their homes to the Hospital even during the induction periods (average cost of each journey estimated €20 for a total of about €8000), but a 20% of our patients during the induction periods are hospitalized. Thus, we have to add the hospitalization cost of at least ten patients for ten days that is approx. €60000 (our daily rate is €600). For tDCS treatment, the total added cost due to the COVID-19 lockdown in our Hospital will be of approx. €120000 (costs assumed by the national health system and insurances plus the costs assumed by the patients). This means that one month lockdown increases our annual cost for NIBS treatment about 50%, considering that in one year, 74 patients usually received an average of 25 maintenance sessions for a total of 1850 sessions and €222000 cumulative costs (NIBS sessions: €185000 and travel expenses: €37000). In conclusion, the COVID-19 lockdown, at least in our Hospital, has a clear negative clinical impact on chronic drug-resistant pain patients treated with NIBS, and implies a substantial extra cost for public health system, insurances and patients.

### Declaration of competing interest

AO and GF co-founded Neurek SL and GF co-founded Newronika Srl.

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