Clinical improvement with intensive robot-assisted arm training in chronic stroke is unchanged by supplementary tDCS

Edwards, Dylan J.

Cortes, Mar

Rykman-Peltz, Avrielle

Chang, Johanna

Elder, Jessica

Thickbroom, Gary

Mariman, Juan J.

Gerber, Linda M.

Oromendia, Clara

Krebs, Hermano I.

Fregni, Felipe

Volpe, Bruce T.

Pascual-Leone, Alvaro

Background: Intensive robot-assisted arm training in the chronic phase of stroke recovery can lead to clinical improvement. Combinatorial therapeutic approaches are sought to further optimize stroke recovery. Transcranial direct current stimulation (tDCS) is one candidate to combine with robotic training, as transient increases in excitability and improvements in motor behavior have separately been reported. Objective: To determine whether tDCS, delivered prior to robotic training, could augment clinical improvement. Methods: We conducted a dual-site, randomized controlled trial in 82 chronic ischemic stroke patients (inclusion > 6 m post-injury, dominant hemisphere, first stroke; residual hemiparesis) who were split into two groups to receive tDCS (M1-SO montage, anode ipsilesional, 5×7 cm electrodes, 2 mA, 20 mins) or sham tDCS, prior to robotic upper-limb training (12 weeks; 36 sessions; shoulder-elbow robot or wrist robot on alternating sessions). The primary end-point was taken after 12 weeks of training, and assessed with the Upper Extremity Fugl-Meyer

impairment scale (FM). Corticomotor conduction was assessed with transcranial magnetic stimulation (TMS). Results: For the combined group (n = 82; post-training) robotic training increased the FM by 7.36 points compared to baseline ($p < 0.0001$). There was no difference in the FM increase between the tDCS and sham groups (6.97 and 7.73 respectively, $p = 0.46$). In both groups, clinically meaningful improvement (?5 points) from baseline was evident in the majority of patients (56/77), was sustained six months later (54/72), and could be attained in severe, moderate and mild baseline hemiparesis. Clinical improvement was associated with increased excitability in the affected hemisphere as assessed by resting motor threshold (pre-post $p = 0.029$; pre-post 6 months $p = 0.029$), but not with threshold-adjusted assessment of MEP amplitude (pre-post $p = 0.09$; pre-post 6 months $p = 0.15$). Participants with motor evoked potentials were more likely to improve clinically than those without (17/18, 94%, versus 39/59, 66%, $p = 0.018$). Conclusions: Our study confirms the benefit of intensive robot-assisted training in stroke recovery, and indicates that conventional tDCS does not confer further advantage to robotic training. We also showed that corticospinal integrity, as assessed by TMS, is a predictor of clinically meaningful response to intensive arm therapy in chronic stroke.