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# Propriospinal cutaneous-induced EMG suppression is unaltered by anodal tDCS of healthy motor cortex

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HIGHLIGHTS

- Propriospinal excitability was not affected by M1 a-tDCS in ipsilateral or contralateral arms.
- Anodal tDCS with 1 mA or 2 mA current intensity did not affect propriospinal excitability.
- The effect of tDCS on propriospinal excitability was not altered by unilateral vs bilateral tasks.

ABSTRACT

*Objective:* Cervical propriospinal premotoneurons (PN) relay descending motor commands and integrate peripheral afferent feedback. Effects of anodal transcranial direct current stimulation (a-tDCS) on propriospinal excitability in the upper limbs are unknown.
*Methods:* Healthy right-handed adults received a-tDCS or sham tDCS over primary motor cortex (M1) at 1 mA (Experiment 1, $n = 18$) or 2 mA current intensity (Experiment 2, $n = 15$). Propriospinal excitability was assessed by suppression of background electromyography (EMG) in extensor carpi radialis (ECR) from electrical stimulation of the superficial radial nerve during bilateral (Experiment 1 and 2) or unilateral (Experiment 2 only) activation of the left and/or right ECR. EMG suppression could be attributed to an early propriospinal component and late cortical component. Motor evoked potentials (MEP) were obtained as a manipulation check.
*Results:* Before tDCS, propriospinal-mediated cutaneous-induced suppression was present in each arm for early and late components. ECR MEP amplitude increased after 1 mA, but not 2 mA, a-tDCS. Neither 1 mA nor 2 mA a-tDCS modulated either component of ipsilateral or contralateral propriospinal excitability during bilateral or unilateral tasks.
*Conclusions:* Propriospinal-mediated cutaneous-induced suppression was not modulated by a-tDCS in healthy adults.
*Significance:* Reporting non-significant findings is paramount for the development of clinically-relevant tDCS protocols.


## 1. Introduction

Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique with potential application as an adjuvant to neuro-rehabilitation of the upper limb. Anodal tDCS (a-tDCS) is expected to increase corticomotor excitability and cathodal tDCS (c-tDCS) decrease corticomotor excitability (Nitsche and Paulus, 2000; Nitsche et al., 2008; Stagg and Nitsche, 2011). The exact mechanisms of tDCS are yet to be elucidated, however corticomotor excitability may be modulated via acute subthreshold shifts in the membrane potential that mediates polarity-specific changes in synaptic plasticity (Stagg and Nitsche, 2011). Imaging and computational modelling studies show the effects of tDCS in the conventional electrode montages are not limited to cortical regions directly beneath the stimulating electrodes, but show widespread effects throughout the brain, including both cortical and subcortical structures (Lang et al., 2005; Zheng et al., 2011; Bikson et al., 2012; Datta et al., 2012). Understanding the effects tDCS has on various neural structures that contribute to movement of the upper limb will be important for future clinical applications.

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Propriospinal premotoneurons (PNs) at the cervical 3rd and 4th (C3-C4) segmental level of the spinal cord are essential for accurate control of the upper limb (Sasaki et al., 2004; Alstermark et al., 2011; Kinoshita et al., 2012). Descending motor commands from contralateral and ipsilateral M1 are relayed through PNs in parallel with direct corticospinal activation of α-motoneurons (αMNs) (Fig. 1) (Illert et al., 1978, 1981; Mazevet et al., 1996, Pierrot-Deseilligny, 1996; Nicolas et al., 2001; Pierrot-Deseilligny and Burke, 2005; Boudrias et al., 2010). In humans and non-human primates, descending inputs to spinal inhibitory interneurons (INs) tonically inhibit PNs that are released for goal-directed upper limb movements such as reaching (Alstermark et al., 1999; Nicolas et al., 2001; Pierrot-Deseilligny and Burke, 2005; Isa et al., 2006; Giboin et al., 2012). PNs studied in the cat, have divergent projections onto multiple αMNs that presumably assist multi-joint co-ordination of proximal and distal upper limb muscles, as well as agonist and antagonist pairs (Alstermark et al., 1990; Pierrot-Deseilligny, 1996; Pierrot-Deseilligny and Burke, 2005). In humans, PNs receive sensory input from the periphery (Fig. 1), which allows prompt integration of sensory feedback to rapidly update descending motor commands (Burke et al., 1992; Pierrot-Deseilligny, 1996; Pierrot-Deseilligny and Burke, 2005; Roberts et al., 2008). These distinct features likely make C3-C4 PNs essential for coordinating goal-directed upper limb movement.

The excitability of C3-C4 PNs in humans can be inferred non-invasively using different protocols, such as cutaneous-induced suppression or peripheral nerve-conditioned transcranial magnetic stimulation (TMS). Cutaneous-induced suppression involves applying trains of electrical stimulation to the superficial radial nerve (SRN) during weak voluntary wrist extension. Superficial radial nerve stimulation activates a cutaneous afferent pathway that induces a period of suppression in the on-going electromyography (EMG) with a long central delay (Fig. 2). The central delay becomes longer the more caudal the motor neuron pool, thus indicating EMG suppression is mediated by neurons located above the αMN such as C3-C4 PNs. Suppression of the EMG is likely due to disfacilitation of αMNs via PNs rather than inhibition exerted directly onto

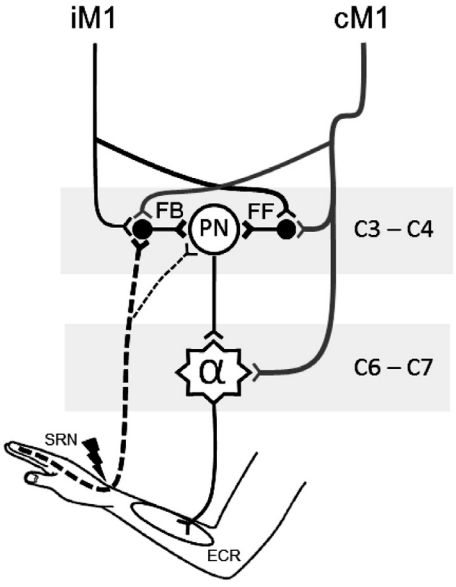


**Fig. 1.** Simplified schematic of the ipsilateral (iM1) and contralateral (cM1) motor inputs to C3 – C4 propriospinal system and experimental configuration. Peripheral nerve stimulation was delivered to the superficial radial nerve (SRN) at the wrist, directing cutaneous afferent input to inhibitory interneurons (IN, closed circle) that inhibit C3-C4 propriospinal neurons (PN), and disfacilitate extensor carpi radialis (ECR) α-motoneurons (α). All projections are excitatory except for feedforward (FF) and feedback (FB) INs. Grey boxes indicate C3-C4 and C6-C7 level of the spinal cord.

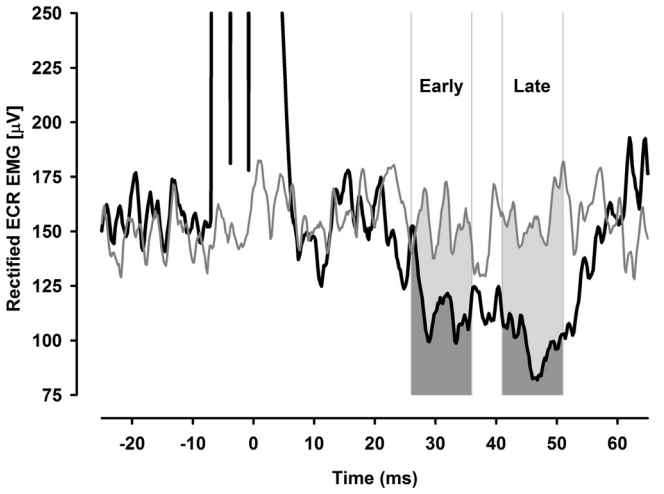


**Fig. 2.** Rectified EMG from the ECR of a representative subject. The average conditioned (C) trace (black line) is shown overlying the non-conditioned (NC) trace (grey line). The last pulse of the train of electrical stimulation to the SRN was delivered at time 0. The area under the curve was measured for the early component between 26 ms and 36 ms, and late cortical component between 41 and 51 ms for each NC (light grey shading) and C (dark grey shading) trial. The trace is an average of 150 NC and 150 C trials.

αMNs (Pierrot-Deseilligny, 1996) because the monosynaptic H-reflex is relatively un-affected by SRN stimulation, whereas TMS-evoked responses are suppressed by SRN stimulation (Burke et al., 1994). An SRN-conditioned motor evoked potential (MEP) shows an unaffected initial monosynaptic component suggesting inhibition of the αMN is indirect (Mazevet et al., 1996; Pierrot-Deseilligny, 1996). In this manner, cutaneous-induced suppression can be used to investigate the functional relevance of C3-C4 PNs in humans.

Previous studies have shown tDCS can modulate cervical propriospinal excitability in the ipsilateral arm of healthy adults (Bradnam et al., 2011; McCambridge et al., 2014). In these studies, peripheral nerve-conditioned TMS was used to evoke facilitation and inhibition components of propriospinal excitability before and after c-tDCS or dual-hemisphere tDCS with the cathode positioned over the ipsilateral M1. Cathodal tDCS suppressed both components of propriospinal excitability in the ipsilateral arm (Bradnam et al., 2011), whereas dual-hemisphere tDCS suppressed the facilitation component whilst maintaining inhibition (McCambridge et al., 2014). To date, no study has investigated the effects of a-tDCS on C3-C4 propriospinal excitability in the upper limb.

While tDCS modulates M1 neuronal excitability in a polarity-dependent manner (Nitsche et al., 2008), its effects on subcortical and spinal neurons is not completely understood. Based on c-tDCS effects described above, we hypothesised that propriospinal excitability would increase bilaterally after left M1 a-tDCS. This was examined in the extent of SRN-induced EMG suppression during a bilateral and unilateral contraction of the left and/or right ECR, which we expected would increase after 1 mA and 2 mA a-tDCS. As a manipulation check, MEPs were collected from the right ECR and APB which we hypothesised would be facilitated after a-tDCS but not sham stimulation.

## 2. Methods

### 2.1. Study design

The study was divided into two experiments. For each experiment participants completed two double-blinded sessions, receiv-