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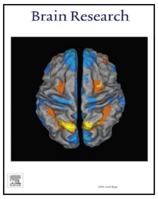

Research report

Electroencephalography correlates of transcranial direct-current stimulation enhanced surgical skill learning: A replication and extension study

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HIGHLIGHTS

- Application of anodal tDCS concurrent to surgical training enhances unimanual skill acquisition compared to training alone.
- Changes in delta EEG activity in the sensorimotor network are associated with surgical skill improvement.
- EEG patterns of unimanual and bimanual surgical skill performance differ, primarily within the parietal cortex.
- Anodal tDCS modulated alpha frequency band activity during bimanual surgical skill performance.

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ABSTRACT

Transcranial direct-current stimulation (tDCS), an increasingly applied form of non-invasive brain stimulation, can augment the acquisition of motor skills. Motor learning investigations of tDCS are limited to simple skills, where mechanisms are increasingly understood. Investigations of meaningful, complex motor skills possessed by humans, such as surgical skills, are limited. This replication and extension of our previous findings used electroencephalography (EEG) to determine how tDCS and complex surgical training alters electrical activity in the sensorimotor network to enhance complex surgical skill acquisition. In twenty-two participants, EEG was recorded during baseline performance of simulation-based laparoscopic surgical skills. Participants were randomized to receive 20 min of primary motor cortex targeting anodal tDCS or sham concurrent to 1 h of surgical skill training. EEG was reassessed following training, during a post-training repetition of the surgical tasks. Our results replicated our previous study suggesting that compared to sham, anodal tDCS enhanced the acquisition of unimanual surgical skill. Surgical training modulated delta frequency band activity in sensorimotor regions. Next, the performance of unimanual and bimanual skills evoked unique EEG profiles, primarily within the beta frequency-band in parietal regions. Finally, tDCS-paired surgical training independently modulated delta and alpha frequency-bands in sensorimotor regions. Application of tDCS during surgical skill training is feasible, safe and tolerable. In conclusion, we are the first to explore electrical brain activity during performance of surgical skills, how electrical activity may change during surgical training and how tDCS alters the brain to enhance skill acquisition. The results provide preliminary evidence of neural markers that can be targeted by neuromodulation to optimize complex surgical training.

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1. Introduction

More than 300 million surgical procedures are required to address the global burden of disease (Rose et al., 2015). Meeting this demand necessitates an adequately trained and competent surgical workforce. Recent changes in surgical training have impacted both the cognitive and technical abilities of surgical trainees (Lewis and Klingensmith, 2012; Klingensmith and Lewis, 2013; Griner et al., 2010; Ahmed et al., 2014). For example, surgical program directors believe that many of their senior trainees are incapable of operating independently (Mattar et al., 2013) while many trainees are not confident in their ability to operate effectively (Coleman et al., 2013). One important factor that may contribute to this shortcoming is the implementation of work-hour restrictions, which has limited the hands-on time that surgical trainees spend training their technical skills. Trends in patient outcomes suggest that the implementation of surgical trainee work-hour restrictions may be associated with a rise in patient morbidity and mortality (Ahmed et al., 2014; Churnin et al., 2016; Browne et al., 2009), as well as an overall negative impact on resident education (Griner et al., 2010; Ahmed et al., 2014; Churnin et al., 2016; Browne et al., 2009; Bolster and Rourke, 2015). Many other factors that may hinder trainees from achieving surgical competence have also been identified, including: limited opportunities for trainees to practice technical skills in both clinical and simulation-based environments, lack of structured and adequate feedback from trainers, as well as poor curriculum design (Lewis and Klingensmith, 2012). Improving and optimizing the current state of surgical training, in an era of reduced hands-on training, is therefore vital.

Transcranial direct-current stimulation (tDCS) is an increasingly applied form of non-invasive brain stimulation (Bikson et al., 2016). By passing weak electric current across the scalp, tDCS modulates cortical excitability and may induce lasting changes in primary motor cortex (M1) plasticity (Nitsche and Paulus, 2000). When M1 excitability is modified by tDCS concurrent with motor training, there is often a marked enhancement of skill acquisition (Reis et al., 2009). This evidence is largely based on simple tasks rather than more complex motor skills possessed by humans. Recently, we demonstrated that the application of tDCS concurrent to complex laparoscopic (Ciechanski et al., 2018) and neurosurgical skill training (Ciechanski et al., 2017) resulted in an enhanced rate of skill acquisition. The neural mechanisms underlying such motor skill enhancement by tDCS remain poorly understood. The use of tools such as electroencephalography (EEG), which can measure electrical activity of the brain, may be able to elucidate the changes in brain dynamics induced by motor skill training and neurostimulation. Identifying the neural correlates of surgical skill training, and subsequently its enhancement by tDCS, may guide the optimization of targeted neuromodulation to enhance skill acquisition.

The aims of this study were to: 1) replicate our previous findings suggesting that tDCS may potentially enhance laparoscopic surgical skill acquisition, 2) identify changes in electrical activity in sensorimotor areas during laparoscopic surgical training, 3) identify differences in the EEG frequency band power between unimanual and bimanual laparoscopic surgical task performance, and 4) identify how tDCS modulates the sensorimotor areas to enhance surgical skill acquisition. Given our previous investigations (Ciechanski et al., 2018), we hypothesized that tDCS would enhance the acquisition of unimanual, but not bimanual, laparoscopic surgical skills. Based on prior investigations of simple motor movements (Tomiak et al., 2017), we hypothesized that unimanual and bimanual task performance would produce distinct EEG patterns. We also hypothesized, based on previous EEG studies of motor tasks (Mathewson et al., 2012; Wu et al., 2014; Deeny et al., 2009; Pfurtscheller et al., 1996; Aoki et al., 2001, 1999; Harmony, 2013; Wong et al., 2014; Picazio et al., 2014, 2011; Jochumsen et al., 2017), that high-beta (β), alpha (α), and delta (δ) EEG power would be altered following task training, with tDCS producing unique effects. In this study, participants received anodal or sham tDCS concurrent to training to perform two simulation-based laparoscopic surgery skills. Task-based EEG was recorded concurrently. Findings from this study would serve to advance the application of non-invasive brain stimulation to enhance complex surgical skill learning.

Table 1
Demographics and baseline characteristics. SD, standard deviation.

	Sham tDCS (n = 11)	Anodal tDCS (n = 11)
Mean age (SD)	25.5 (4.7) years	25.9 (3.6) years
Sex ratio (M:F)	8:3	8:3
Handedness (right:left)	11:0	10:1
Mean interest in surgery (SD)	5.9/10 (2.8)	6.9/10 (2.1)
Mean pattern cutting score (SD)	146.9 (30.2)	140.0 (51.4)
Mean peg transfer score (SD)	95.5 (55.7)	97.5 (51.2)

2. Results

2.1. Demographics

Twenty-two medical and veterinary students were recruited. Population characteristics and baseline surgical performance scores are shown in Table 1. Baseline characteristics were not different between groups (all $t_{20} < 0.948$, $p > 0.354$). Correlation between population characteristics and baseline surgical performance revealed a significant correlation between the number of hours of sleep the previous night and baseline pattern cutting score ($r = 0.429$, $p = 0.046$), where those that reported a longer duration of sleep the night before demonstrated better performance; there was no significant correlation however between self-reported tiredness levels and baseline pattern cutting score. A significant correlation was also observed between baseline pattern cutting and baseline peg transfer scores ($r = 0.487$, $p = 0.010$), where those that performed better on one task were more likely to perform better on the other task.

2.2. Effects of tDCS on surgical skill learning

Pattern cutting learning curves are shown in Fig. 1A. All participants improved their pattern cutting scores over the training period ($F_{1,20} = 983.459$, $p < 0.001$). A significant intervention effect suggested that participants receiving anodal tDCS (64.5 ± 6.0%) had larger improvements compared to those receiving sham (53.6 ± 10.9%; $t_{20} = 2.796$, $p = 0.010$). Subsequent pre-specified analysis delineated low and high-skill performers based on their baseline scores (Ciechanski et al., 2017). Low-skill participants receiving anodal tDCS showed larger improvements in pattern cutting compared to those receiving sham (Supplementary Fig. 3A; $U = 27.000$, $p = 0.030$). Weaker, non-significant effects of tDCS intervention were seen in the high-skill participants ($U = 24.000$, $p = 0.126$).

Peg transfer learning curves are shown in Fig. 1B. All participants improved their peg transfer scores over the training period ($F_{1,20} = 550.753$, $p < 0.001$), however there was no significant difference at post-training between participants receiving anodal tDCS (50.0 ± 12.5%) or sham (54.8 ± 7.9%; $t_{20} = 1.073$, $p = 0.296$). No significant intervention effects on peg transfer were seen when participants were classified as low- or high-skill performers (Supplementary Fig. 3B). Raw pattern cutting and peg transfer scores, in contrast to percent change from baseline, yielded similar results to those outlined above (Supplementary Fig. 4).

2.3. Effects of surgical training on EEG patterns

We performed an exploratory examination of changes in EEG power following surgical training paired with sham tDCS, mimicking the effects of surgical training alone. Surgical training lead to a significant decrease in δ power between baseline and post-training pattern cutting

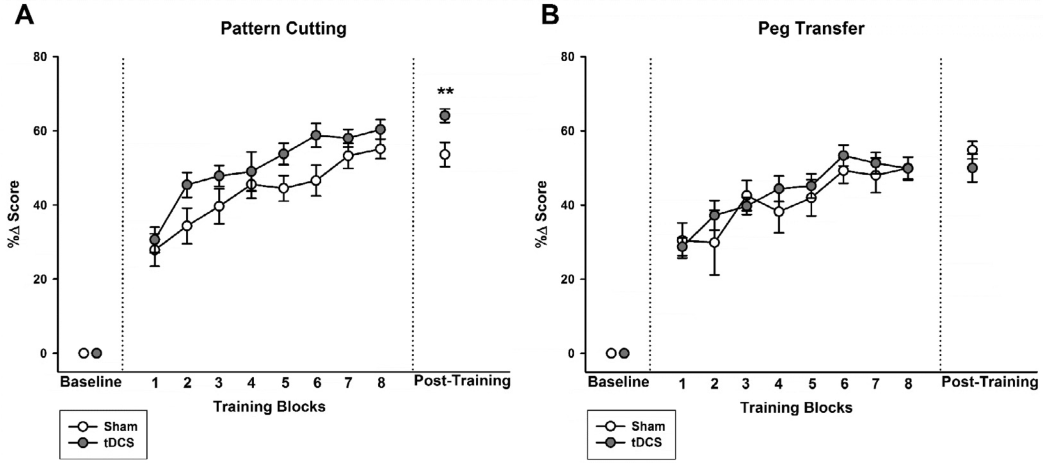

Fig. 1. Learning curves of laparoscopic (1A) pattern cutting and (1B) peg transfer. Participants receiving sham (white circles) and anodal tDCS (grey circles) are shown. Values are mean, and error bars standard error. **$p < 0.01$.

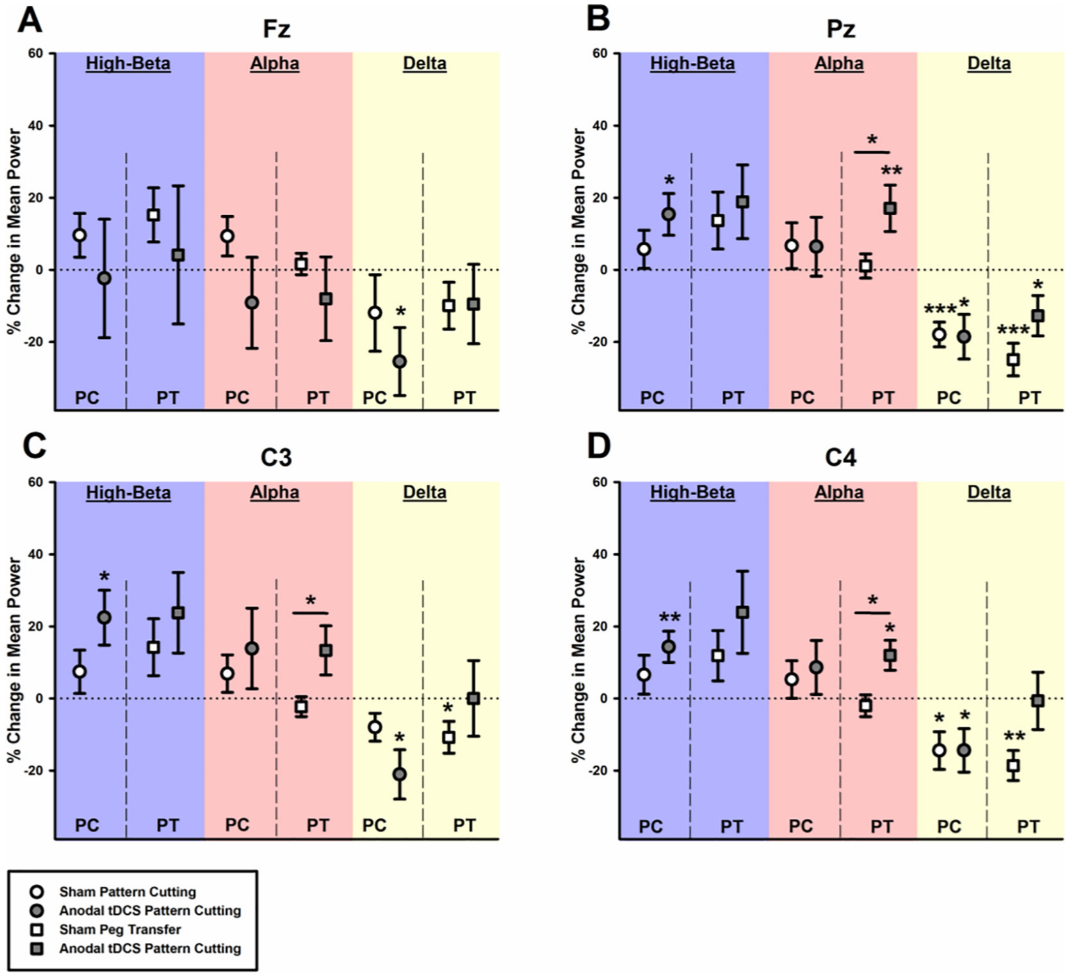

Fig. 2. Average changes between baseline and post-training EEG power in high-beta (blue), alpha (red) and delta (yellow) frequency bands. Changes with sham (white) or anodal tDCS (grey) for pattern cutting (PC; circles) and peg transfer (PT; squares) are shown. Significance asterisks above symbols indicate significant increases or decreases from a 0% change. Significance stars above horizontal lines indicate significant differences between groups. Values are means and error bars represent standard error. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

($F_{1,10} = 11.719$, $p = 0.007$; Fig. 2) and peg transfer performance ($F_{1,10} = 14.779$, $p = 0.003$). Post-hoc measures demonstrated significant decreases in δ power during pattern cutting at electrodes Pz and C4 (both $t_{10} > 2.762$, $p < 0.021$), and during peg transfer at electrodes C3, Pz, and C4 (all $t_{10} > 2.431$, $p < 0.036$). Our exploratory analysis did not reveal any significant changes in β frequency power during pattern cutting ($F_{1,10} = 1.907$, $p = 0.197$) or peg transfer performance ($F_{1,10} = 3.656$, $p = 0.085$), nor in α frequency power during pattern cutting ($F_{1,10} = 1.764$, $p = 0.214$) or peg transfer performance ($F_{1,10} = 0.359$, $p = 0.860$).

Table 2

Baseline EEG power during laparoscopic pattern cutting or peg transfer tasks. Columns display power within various frequency bands. Rows display power at a specified electrode location. Values indicate mean with standard deviation in brackets. *p < 0.05, **p < 0.01, ***p < 0.001.

Task	Electrode	α Power (uV^2)	β Power (uV^2)	δ Power (uV^2)	Between Task Differences
Pattern Cutting	Fz	0.274 (0.100)	0.159 (0.078)	1.795 (0.547)	n.s.
	Pz	0.265 (0.094)	0.151 (0.069)	1.601 (0.679)	β*
	C3	0.194 (0.076)	0.137 (0.071)	1.311 (0.575)	n.s.
	C4	0.192 (0.078)	0.144 (0.084)	1.311 (0.612)	n.s
Between Electrode Differences		Fz vs C3* Fz vs C4** Pz vs C3*** Pz vs C4***	n.s.	Fz vs C3** Fz vs C4** Pz vs C3*** Pz vs C4***	
Peg Transfer	Fz	0.292 (0.119)	0.146 (0.075)	1.853 (0.652)	
	Pz	0.273 (0.094)	0.136 (0.068)	1.711 (0.843)	
	C3	0.203 (0.081)	0.133 (0.080)	1.383 (0.665)	
	C4	0.201 (0.085)	0.138 (0.091)	1.377 (0.688)	
Between Electrode Differences		Fz vs C3** Fz vs C4** Pz vs C3*** Pz vs C4***	n.s.	Fz vs C3** Fz vs C4*** Pz vs C3** Pz vs C4**	

2.4. Unimanual vs bimanual surgical performance EEG patterns

EEG was recorded concurrent to baseline surgical task performance. One participant, randomized to the anodal tDCS condition, was excluded from the EEG analysis due to poor quality EEG signal. As no intervention had been applied at this point, participants randomized to anodal and sham tDCS conditions were grouped as part of the analysis. In this exploratory analysis, frequency bands of sensorimotor regions were analyzed to determine differences in power during performance of unimanual versus bimanual laparoscopic tasks. In the β band, power was not significantly different between sampled electrodes (Table 2). In the α band, there was a significant difference in power during pattern cutting ($F_{1.322,26.441} = 12.077$, $p = 0.001$), with both Fz and Pz demonstrating higher power than C3 and C4 (all $p < 0.016$). Similarly, significant differences were seen in the α band during peg transfer ($F_{1.301,26.030} = 15.246$, $p < 0.001$), again with Fz and Pz showing greater power than C3 and C4 (all $p < 0.005$). In the δ band, there was a significant difference in power between electrodes for pattern cutting ($F_{1.682,33.631} = 16.726$, $p < 0.001$), with greater power at both Fz and Pz than at C3 and C4 (all $p < 0.002$). Similar significant differences were seen for peg transfer in the δ band ($F_{2.247,44.947} = 16.493$, $p < 0.001$), again with Fz and Pz showing greater power than C3 and C4 (all $p < 0.006$). In all electrodes, power was greatest in the δ band, followed by the α band, and finally the β band.

In the β band, power was significantly different between pattern cutting and peg transfer ($F_{3,18} = 2.997$, $p = 0.038$). Post-hoc evaluation suggested that Pz showed greater β power during pattern cutting compared to peg transfer tasks ($t_{20} = -2.267$, $p = 0.035$). Neither α nor δ bands showed a difference in power between the two tasks.

To examine a relationship between power and baseline task performance, we performed a correlation analysis. We did not find any significant correlations between baseline power and baseline task performance. The strongest correlation of baseline pattern cutting performance was with α frequency power at electrode Fz ($r = -0.378$, $p = 0.091$; Supplementary Fig. 2A). The strongest correlation of baseline peg transfer performance was with δ frequency power at electrode Pz ($r = -0.298$, $p = 0.189$; Supplementary Fig. 2B).

2.5. Effects of tDCS supplemented surgical training on EEG patterns

For this exploratory analysis we examined changes in power across various EEG frequencies following training supplemented with anodal tDCS (Fig. 2). EEG recorded during pattern cutting performance revealed a significant increase in β power ($F_{1,19} = 12.826$, $p < 0.001$), and α power ($F_{1,19} = 4.533$, $p = 0.035$) between baseline and post-training. There were no significant interventional effects for both β ($F_{1,19} = 0.863$, $p = 0.354$) and α frequencies during pattern cutting ($F_{1,19} = 0.139$, $p = 0.709$). At post-training, there was also a significant decrease in δ power during pattern cutting ($F_{1,19} = 60.900$, $p < 0.001$). Again, there was no significant effect of intervention on the magnitude of decrease in δ power from baseline to post-training during pattern cutting ($F_{1,19} = 2.898$, $p = 0.091$), however δ power at all electrodes decreased in the anodal tDCS group (all $p < 0.042$), whereas decreased power was only present in Pz and C4 in the sham tDCS group.

EEG recorded during peg transfer performance revealed a significant increase in β power ($F_{1,19} = 17.356$, $p < 0.001$), and α power ($F_{1,19} = 4.163$, $p = 0.043$) between baseline and post-training (Fig. 2). No significant intervention effect was present for β power ($F_{1,19} = 0.272$, $p = 0.603$), however an intervention effect revealed larger increases in α power in participant's receiving anodal tDCS ($F_{1,19} = 5.025$, $p = 0.026$). Post-hoc measures revealed significantly larger increases in α power with tDCS compared to sham at C4 ($t_{19} = 2.764$, $p = 0.012$), Pz ($t_{19} = 2.263$, $p = 0.036$), and C3 electrodes ($t_{19} = 2.205$, $p = 0.040$). With peg transfer there was an overall decrease in δ power between baseline and post-training ($F_{1,19} = 18.710$, $p < 0.001$), with significant intervention effects ($F_{1,19} = 4.218$, $p = 0.042$) suggesting larger reductions in participants receiving sham tDCS concurrent to training.

2.6. Correlation between surgical skill learning and EEG changes

Finally, we evaluated change in task score compared to change in frequency band power. Change in pattern cutting score was correlated with the change in α power at Fz ($r = -0.492$, $p = 0.023$; Fig. 3A), change in β power at C4 ($r = 0.449$, $p = 0.041$), and δ power at Fz ($r = -0.428$, $p = 0.053$). Change in δ power at Pz was negatively correlated with change in peg transfer score ($r = -0.560$, $p = 0.008$; Fig. 3B), with correlations also evident at C3 ($r = -0.473$, $p = 0.031$).

2.7. Safety and tolerability

All procedures were well-tolerated and no adverse effects of tDCS were reported. Tingling (59%), itching (32%), and warmness under the electrodes (23%) were the only reported sensations (Table 3). There was no difference in the proportion of participants reporting presence of sensations in either anodal tDCS or sham conditions (all sensations $p > 0.170$). Likewise, there was no difference in the severity of sensations reported between intervention groups (all sensations $p > 0.320$). All sensations were ranked as 'mild'. Correct stimulation allocation guesses were made 36% of the time, worse than chance guessing.

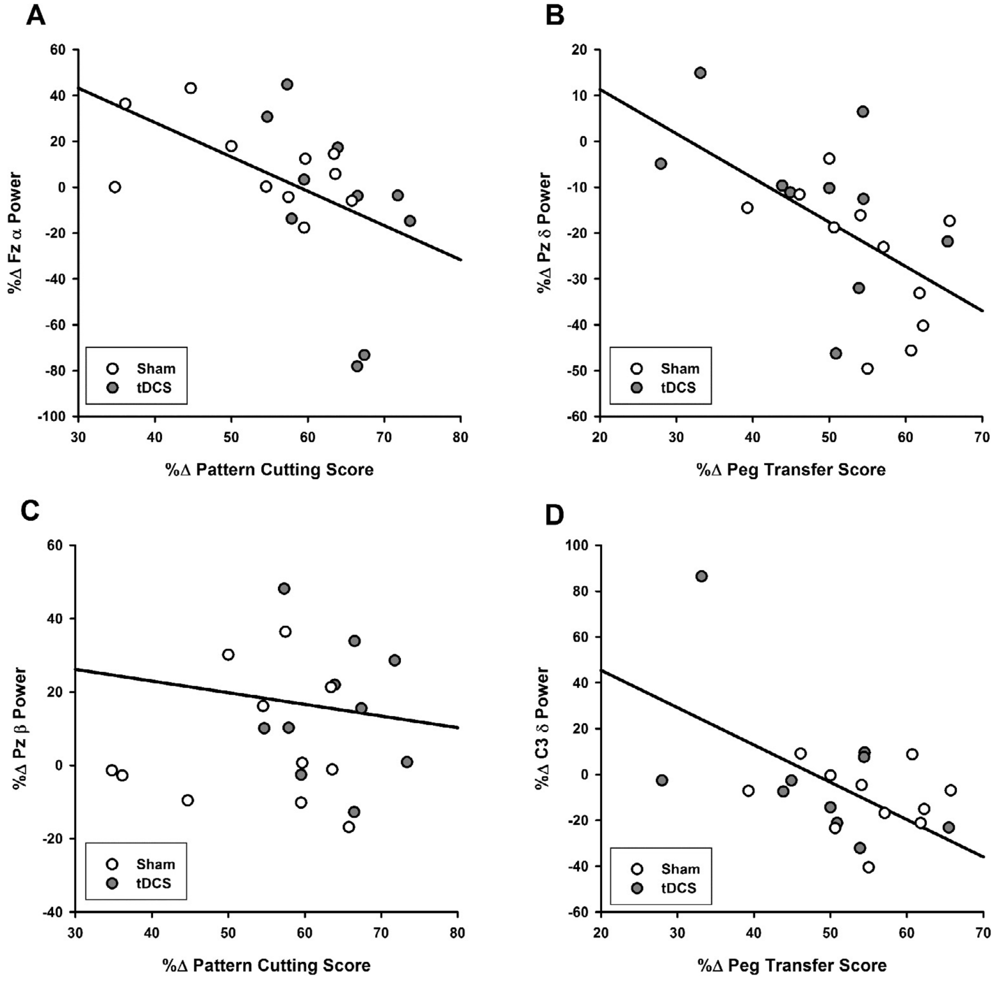

Fig. 3. Correlation between change in α power at electrode Fz and change in pattern cutting scores (3A), change in δ power at electrode Pz and change in peg transfer score (3B), change in β power at electrode Pz and change in pattern cutting score (3C), and change in δ power at electrode C3 and change in peg transfer score (3D). White circles represent participants receiving sham tDCS, and grey circles anodal tDCS.

Table 3
Sensation and tolerability of transcranial direct-current stimulation (tDCS).

	Proportion of participants reporting sensation			VAS sensation severity ranking (0–5)		
	Sham tDCS	Anodal tDCS	*P*-value	Sham tDCS	Anodal tDCS	*P*-value
Itching	2/11	5/11	0.17	0.18 (0.40)	0.43 (0.72)	0.33
Tingling	6/11	7/11	0.67	0.82 (0.98)	1.00 (1.03)	0.68
Warmness	3/11	2/11	0.61	0.64 (1.10)	0.34 (1.09)	0.53
Headache	0/11	0/11	1.00	0	0	1.00
Lightheadedness	0/11	0/11	1.00	0	0	1.00
Neck pain	0/11	0/11	1.00	0	0	1.00
Toothache	0/11	0/11	1.00	0	0	1.00
Tinnitus	0/11	0/11	1.00	0	0	1.00
Visual disturbances	0/11	0/11	1.00	0	0	1.00

3. Discussion

In this study, we replicated our previous findings that supplementing surgical training with tDCS enhances the acquisition of laparoscopic skills. Application of tDCS towards surgical skill learning is among the most complex motor skills investigated. Extending our previous investigations, we explored how electrical activity may change during surgical training, differences in electrical brain activity during performance of unimanual and bimanual surgical skills, and how tDCS may alter electrical activity of the brain to enhance skill acquisition. Trials such as these serve to identify neural markers that can be targeted by neuromodulatory technologies to optimize learning.

In the current study, using a similar but not identical tDCS montage, we replicated our previous findings (Ciechanski et al., 2018), suggesting that tDCS applied concurrent to surgical training enhances skill acquisition. Our work expanded these findings, showing that both trainees with low and high-basal skill may be susceptible to the effects of tDCS. These encouraging findings suggest utility of tDCS even in higher skill residents or fellows. As in our previous investigation, our current findings confirmed that unimanual skills, such as laparoscopic pattern cutting, are more sensitive to the modulatory effects of tDCS, compared to bimanual peg transfer skills. We hypothesize that because conventional tDCS modulates only the targeted M1, while bimanual skills utilize both M1, peg transfer skill is less sensitive to enhancement due to under-dosing of the non-dominant M1. The relationship between cortical electric field strength and behavioral effects is unclear however. In our previous investigations, we demonstrated larger effects of tDCS on peg transfer skill acquisition than here. Our current-modeling suggests that the modified ring-electrode montage induces stronger electric fields in the targeted M1, compared to the conventional sponge montage utilized previously. Furthermore, conventional sponge techniques induce stronger electric fields in the contralateral frontal lobe. These differences in electric field patterns may produce dissimilar behavioral effects, but suggest that the non-dominant hemisphere is a crucial target of tDCS for enhancing complex bimanual motor skills.

Our EEG findings also suggest that the non-dominant M1, in addition to other nodes of the sensorimotor network play a role in surgical skill learning in both unimanual and bimanual tasks. Surgical training alone, as assessed by our sham group, was associated with reduced δ power across the sensorimotor network. Prior investigations of basic visuo-motor skill training suggest that δ power decreases as skill increases (Wong et al., 2014). This decrease may reflect a conversion from the early explicit stages of learning to implicit learning, as task familiarity increases. Our findings reveal that δ activity decreased with training, as task performance shifted from conscious explicit to more automatic forms. This is akin to any motor skill, such as riding a bicycle; conscious effort is required in the early stages of skill learning, however as the skill becomes familiar, implicit processes take over (Dayan and Cohen, 2011). Investigations by others have demonstrated that δ oscillations, but not β or α oscillations, are associated with intrinsic motor representations and movement selection (Hamel-Thibault et al., 1991. 2018; Saleh et al., 2010). These oscillations primarily originate from nodes of the sensorimotor network (Hamel-Thibault et al., 1991. 2018). Our findings support this, as we demonstrated that surgical training itself often altered δ power in the sensorimotor network. We hypothesize that this alteration may relate to the development of motor representations for novel surgical motor skills, where there is a shift from explicit to implicit motor processes to complete surgical tasks. The magnitude of change in δ power was correlated with the change in laparoscopic skills, where greater reductions in power were correlated with larger skill improvements. Therefore, the skill enhancing effects of tDCS may be driven by the ability to develop motor representations more effectively.

Beyond changes in δ activity, we also demonstrated tDCS-dependent changes in β power. Notably, we found that participants receiving anodal tDCS concurrent to training increased β power in areas underlying C3. These increases were most evident during pattern cutting; whereas training alone (sham) did not significantly affect β power, anodal tDCS increased power. Electrode C3 represents the dominant M1, which plays a key role in motor function and learning (Wolpert et al., 2011). Furthermore, the β frequency has long been regarded as an important sensorimotor rhythm (Jasper and Penfield, 1949). Therefore, it is plausible that tDCS increased β activity in M1 to improve surgical performance. Interestingly, there were trending, but non-significant, increases in β activity with surgical training alone, which supports the notion that sensorimotor training may increase β activity, and tDCS is capable of enhancing this signal. These changes were particularly evident with pattern cutting, which may preferentially engage the tDCS-targeted dominant hemisphere. Our findings of changes in β activity remain exploratory in nature, as we did not provide a directed hypothesis regarding EEG changes, future investigations may wish to direct their focus on changes in β activity associated with surgical or complex motor training. Animal studies suggest that tDCS amplifies long-term potential synaptic plasticity via brain-derived neurotrophic factor (BDNF)-dependent changes in the motor cortex to enhance motor learning (Fritsch et al., 2010). Whether these cellular mechanisms of learning are linked to β oscillatory activity has yet to be established, however investigations by others have found associations between β power and serum BDNF concentrations (Kim et al., 2018). Whether tDCS alters β oscillatory activity to promote BDNF release leading to enhanced learning requires further investigation.

Changes in neural activity at C4 were correlated with the amount of skill acquisition. Recent evidence has demonstrated that oscillatory β activity within prefrontal regions is important in inhibiting motor plans to be executed by the M1 (Picazio et al., 2014). With laparoscopic pattern cutting, the non-dominant hand acts as a stabilizer; therefore, increased movements of the stabilizer hand would worsen performance on the task. We found a strong correlation between β power at C4 and pattern cutting improvements, suggesting that stronger motor suppression by nearby non-dominant premotor areas may improve instrument stabilization in laparoscopic environments, leading to better performance. This suppression may be strengthened by tDCS, given that the induced electric fields were relatively strong in the premotor cortex. Future investigations may find interest in examining the effects of reversing the polarity of tDCS, from anodal to cathodal stimulation, on β power, and how this relates to surgical skill learning. This is particularly interesting as conventionally cathodal tDCS is targeted over the non-dominant M1 (i.e. C4), where there were correlations with changes in pattern cutting performance. Direct, head-to-head comparison of anodal and cathodal tDCS, paired with EEG recording, would serve a crucial role in understanding the neural mechanisms underlying the motor enhancing effects of tDCS.

This study is also the first to examine differences in EEG patterns between unimanual and bimanual surgical skill. Our findings suggest that performance of unimanual and bimanual skills both showed greater power at Fz and Pz electrodes, compared to C3 and C4. This was particularly evident in α and δ frequencies. Previous investigations have compared EEG patterns during simple unimanual versus bimanual cyclical movements. Similarly to our findings, others have demonstrated greater α activity at Fz than C3 or C4 during bimanual and unimanual movements (Tomiak et al., 2017). This group also reported that bimanual movements produced distinct α activity from dominant hand movements. Our findings differ, as we demonstrated that the unique patterns of dominant and bimanual hand movements lie within the β band, the sensorimotor band. Our distinct finding may be related to the notion that discrete movements evoke activity linked to recruitment of higher cortical areas, unlike simple cyclical movements (Schaal et al., 2004). The difference in β activity between tasks was greater at electrode Pz, which corresponds to the medial aspect of the superior posterior parietal cortex (PPC). The PPC plays a role in integrating visual input from the visual cortex (Andersen, 1989; Andersen and Buneo, 2003), as well as encoding movement plans (Cui and Andersen, 2007; Andersen and Cui, 2009). Given the lack of depth perception involved in laparoscopic environments, users may rely on visual cues to achieve goal movements. Likewise, unique task electric activity at Pz suggests that different laparoscopic movements require unique integration of visual input, environmental cues, and motor plans to successfully perform skills.

Our trial has various potential limitations that may have influenced our results. First, the effects of tDCS on neurophysiological changes are susceptible to many factors, some which were controllable, but others not. One contributor is an individual's genetic profile. One gene, *BDNF* has been well-documented as playing an important role in an individual's response to tDCS, where those possessing a common polymorphism (met66val) show blunted responses to tDCS (Fritsch et al., 2010). We did not perform genetic testing, and therefore we were unable to ascertain which participants were heterozygotes of the polymorphism. Furthermore, the effects of the *BDNF* met66val polymorphism on EEG signal have not been characterized, and we cannot reasonably concur that this did not contribute to the variability of responses. In addition to genetics there are many other factors recognized as contributing to neurophysiological response to tDCS, including: time of day, quality of sleep the night before, pharmacological agents, menstrual cycle, attention, and many others (Guerra et al., 2017). We documented many of these potential contributors to retroactively control for these factors in our analysis. The major limitation of our EEG measures was that we recorded EEG during performance of a complex task. With complex tasks performed over a series of seconds to minutes, it is difficult to specifically capture what an individual is planning or performing at each moment in time; this contrasts with a simple task such as an odd-ball task, where most participants are in a similar brain-state throughout the task. We attempted to control for this dynamic task by using Fast-Fourier Translation analysis, which allowed us to capture activity from the entire duration of the activity. Future studies may wish to explore the effects of tDCS and medical training on EEG responses to time-locked events such as odd-ball or reward positivity tasks, which hold utility in revealing potential mechanisms underlying learning (Williams et al., 2018).

Our promising findings suggest that enhancing the acquisition of surgical skills with tDCS is feasible, safe, and effective, meriting further investigation. The modulation of the larger motor network represents a future potential target for studies applying tDCS in surgical training; optimizing stimulation parameters is necessary to ensure maximal benefit to enhanced learning on a multitude of medical skills. Enhancing the acquisition of surgical skill learning extend well beyond simply performing surgery quicker and with fewer errors, leading to less complications. Surgical residency consists of years of difficult training during which the trainee is expected to gain the skills necessary to practice independently. This training is multifaceted, and in addition to learning to operate, residents are expected to become experts in human anatomy, develop leadership qualities and the ability to effectively integrate into a team, learn to manage patient bleeding, pain and infection, among a multitude of other tasks. The benefits of enhancing surgical technical skill learning therefore permeates beyond the motor skills themselves, as residents would be afforded more time and opportunity to perfect non-technical skills. The cumulative effect of surgical trainees developing their technical skill-set at a quicker rate, and affording time to develop their non-technical skills would undoubtedly lead to trainees graduating with a new-found sense of confidence and the ability to operate independently, safely, and effectively.

In conclusion, here we provided evidence that tDCS can enhance laparoscopic surgical skill learning. We identified cortical regions involved in performing complex surgical skills, how activity in these regions changes with training, and how tDCS may modulate these regions to augment skill acquisition. Future optimization studies focused on modulating these cortical targets may reveal even larger effects of tDCS on motor learning. Establishing the ability of tDCS to enhance medical skill learning holds the potential to help medical trainees achieve skill proficiency quicker, advancing the future of medical training.

4. Materials & methods

4.1. Design

This was a parallel-design, randomized, sham-controlled, double-blind, single-center trial. All participants provided both verbal and written consent. This served as a replication and extension of our previous investigation (Ciechanski et al., 2018). Differences between the two studies are highlighted in Table 4. The University of Calgary Conjoint Health Research Ethics Board approved all methods of the study (REB17-1453).

4.2. Participants

Recruitment emails were sent to medical and veterinary students who had not previously participated in any study involving laparoscopic training (n = 22, convenience sample). This sample was entirely independent from that in our previous investigation (Ciechanski et al., 2018). The surgical skills performed were deemed relevant to both medical and veterinary students interested in pursuing a surgical specialty. At enrollment, participants were screened for tDCS safety criteria (Woods et al., 2016), previous neurological diagnosis, neuroactive medication, previous brain stimulation experiences, and exposure to laparoscopic surgical training. Objectives of the trial and any possible side effects associated with tDCS were described to participants using a standardized script. Baseline characteristics including age, sex, self-reported handedness, interest in surgery, experience using a laparoscopic simulator, and video game and musical instrument habits were recorded. Sleep history, caffeine, alcohol, and medication intake, as well as daily exercise were also recorded. During consent, participants were informed that the top performing participant would receive $70 in coffee gift cards (all received $20 for participating). This incentive was added to motivate participants to perform to the best of their abilities.

4.3. Outcomes

The behavioral outcomes of the study were performance on the Fundamentals of Laparoscopic Surgery (FLS) pattern cutting and peg transfer tasks. The FLS is an American College of Surgeons endorsed program designed to teach surgical residents and fellows the fundamental technical skills required to perform laparoscopic surgery. These two simulation-based tasks are validated surgical skills that are sensitive to improved performance throughout surgical training (Derossis et al., 1998; Sroka et al., 2010; Steigerwald et al., 2015). These tasks require use of both hands, however pattern cutting is largely unimanual, as the non-dominant hand acts as a stabilizer and performs minimal movement. The peg transfer task in contrast is a purely bimanual task, requiring equal use of both hands. Pattern cutting consists of using endoscopic scissors (held in the dominant hand) and a dissector to cut a marked circle from a 10x10-cm piece of two-ply gauze (Fig. 4B). The peg transfer task involves using two dissectors to transfer six plastic pegs from one end of a pegboard to the other end, and then back (Fig. 4C). For both tasks, the *total score* is calculated as the sum of the *time* and *error score* subtracted from a cut-off time of 300 s. The *time score* is the task completion time in seconds. The *error score* for pattern cutting is the percent deviation of a perfectly cut circle. The *error score* for peg transfer is calculated by multiplying the number of pegs that fell from the field of view by 17. This method of scoring is standard practice

Table 4
Comparison of methodology used in the current study versus our original investigations.

	Current Study	Ciechanski et al., *BJS Open*
Trial design	Parallel-design, randomized, sham controlled, double-blind	Parallel-design, randomized, sham controlled, double-blind
Population	Medical and veterinary students	Medical students
FLS tasks	Pattern cutting and peg transfer	Pattern cutting and peg transfer
Training unit	FLS Box Trainer System	FLS Box Trainer System
Training paradigm	Interleaved, 1-minute break between tasks, 5-minute break after the fourth repetition	Interleaved, 1-minute break between tasks
Number of repetitions	1 baseline, 8 training block, 1 post-training	1 baseline, 8 training block, 1 post-training
tDCS unit	Soterix 1x1 stimulator couples to 4x1 adaptor	Neuroconn DC stimulator
Electrodes	Ring electrodes (1 anode, 4 cathodes	Sponge electrodes (1 anode, 1 cathode)
Electrode holder	EEG cap	Head strap
Anode location	CP3 or CP4 (dominant hemisphere)	C3 or C4 (dominant hemisphere)
Cathode location	Surrounding F3 or F4 (contralateral to anode)	Supraorbital area (contralateral to anode)
Conductive conduit	High-viscosity electrolyte gel	Normal saline
Current strength	1 mA	1 mA
Stimulation duration	20 min	20 min
Sham procedure	30 s ramp-up, 30 s ramp-down	45 s ramp-up, hold current for 60 s, 45 s ramp-down
EEG recording	Yes	No
Motivator	Coffee gift card	Coffee gift card

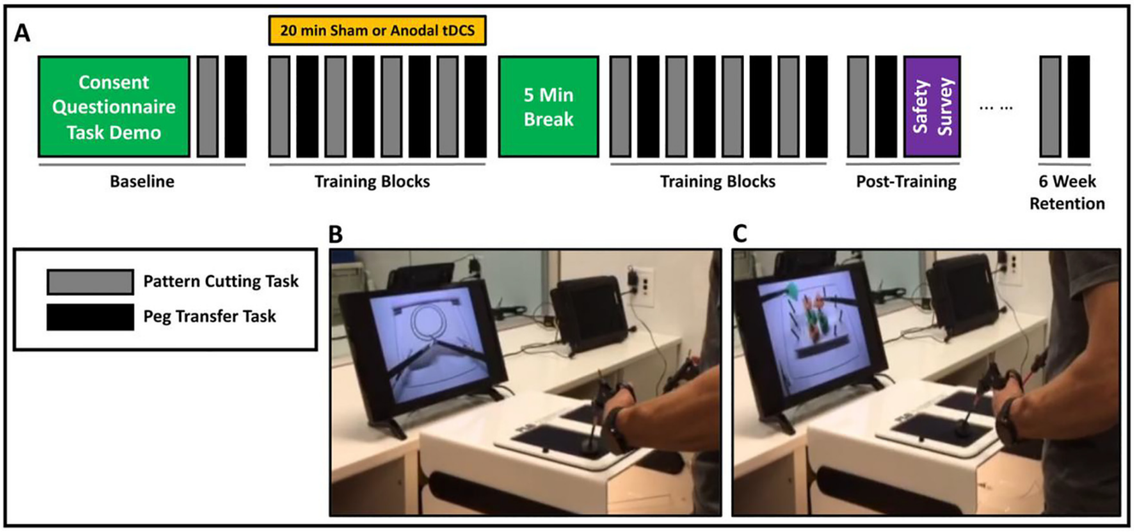

Fig. 4. (4A) Trial design. Participants were fitted with an EEG cap and underwent a baseline evaluation of pattern cutting and peg transfer skills. Training involved eight repetitions of each task, with a break at the midway point. A final repetition of each task was performed at post-training. Participants returned approximately six weeks later to assess retention of skill. (4B) Pattern cutting and (4C) peg transfer skills are shown.

for the FLS tasks (Derossis et al., 1998). All task repetitions were video recorded and then scored by a blinded assessor.

Additional behavioral outcomes included tDCS safety and tolerability. A standard tDCS safety and tolerability questionnaire was completed by participants (Ciechanski et al., 2018), which involved rating the presence and severity of sensations during application of tDCS. Sensations screened included: itching, tingling, headaches, burning or warmness, neck pain, nausea, lightheadedness, tinnitus, and vision or hearing problems. Participants were then asked to guess whether they received the real (anodal) or fake (sham) form of tDCS.

EEG outcomes specifically examined power of β (20–30 Hz), α (8–13 Hz), and δ (0.5–3.5 Hz) frequency bands during performance of pattern cutting and peg transfer tasks. These frequency bands were selected based on previous investigations suggesting their relevance to motor learning (Mathewson et al., 2012; Wu et al., 2014; Deeny et al., 2009; Pfurtscheller et al., 1996; Aoki et al., 2001, 1999; Harmony, 2013; Wong et al., 2014; Picazio et al., 2014, 2011; Jochumsen et al., 2017). EEG was recorded during baseline pattern cutting and peg transfer tasks to examine task specific differences in EEG signal. Baseline EEG patterns were compared to post-training EEG patterns to examine training and tDCS dependent changes in EEG signal. Additionally, as part of this study we also obtained baseline and post-training resting-state EEG, with eyes open, to examine coherence, and event-related potentials from paradigms including the odd-ball task and reward positivity task. The coherence and event-related potential findings are not reported as part of this manuscript, as these are unique outcomes that require further analysis.

4.4. *Trial design*

Trial design is depicted in Fig. 4A. Participants were consented, and computer randomized to the sham or anodal tDCS groups. An EEG cap connected to a 32-lead EEG system (actiCHamp; Brain Products GmbH, Gilching, Germany) was fitted on the participant's head. Next, participants were shown how to perform the FLS tasks using a standardized training demonstration. The tasks were demonstrated visually and described verbally, then participants would confirm whether they understood the instructions. One repetition of each task was performed (baseline) on an FLS Box Trainer System (VTI Medical, Waltham, USA). Following the baseline repetition for each task, stimulation was initiated in both sham and anodal tDCS groups. Stimulation continued for 20 min (or one minute for sham tDCS). Training consisted of eight repetitions of each task, performed in an interleaved manner (A-B-A-B…), which has been suggested to optimize skill learning (Rivard et al., 2015). Following the fourth repetition, a five-minute break was permitted to minimize hand fatigue effects. Following the eighth repetitions, a short break was again permitted. Following this break a final trial of each task was performed (post-training). The EEG cap was then removed, and participants completed the tDCS safety and tolerability questionnaire.

4.5. *EEG acquisition*

Continuous EEG was recorded during baseline and post-training repetitions of pattern cutting and peg transfer. EEG signal was recorded from a 32-lead actiCAP snap active electrode system (Brain Products GmbH), connected to an actiCHamp battery-supplied amplifier (Brain Products GmbH). Electrodes were arranged in a standard 10–20 layout, while electrodes TP9 and TP10 were placed directly on the mastoid processes of the temporal bone. The ground was positioned over Fz. Electrode Cz served as the active reference during recording. Real time recording at a sampling rate of 500 Hz was completed using BrainVision Recorder (ver. 1.21; Brain Products GmbH). To minimize artifact noise, participants were asked to refrain from speaking or clenching their jaw while performing the task. EEG was recorded with the participants' eyes open. Recorded data were stored for offline analysis.

4.6. *EEG analysis*

EEG analysis was performed using BrainVision Analyzer (ver. 2.1; Brain Products GmbH). First, the EEG was segmented into baseline and post-training conditions for pattern cutting and peg transfer tasks. Next, the sampling rate was down-sampled to 250 Hz, and signal re-referenced to electrodes TP9 and TP10. The data was then high-pass filtered at 0.1 Hz and low-pass filtered at 49 Hz. Continuous EEG was segmented into one-second epochs with 50% overlap between epochs. InfoMax independent component analysis (ICA) was applied to identify and remove components associated with blinks. An inverse ICA transformed the data, and then artifact rejection was performed; a trial was discarded when the voltage step in a channel exceeded 10uV/ms or a maximum absolute difference of 100uV was surpassed. If necessary, channels with excessive noise were removed, and interpolated using spherical splines. Fast Fourier transformation, applied with a 10% Hanning window, computed power across frequency bands. Epochs from each condition (baseline vs post-training; pattern cutting vs peg transfer) were averaged for each participant. The average power for β, α, and δ frequency bands was computed. One participant was left-handed, and in this participant, the electrode locations were reflected to allow comparability to the remainder of the right-handed sample (i.e. C3 was regarded to as C4).

4.7. tDCS

The tDCS montage used in this replication study differs from our original study; this change was necessary to accommodate concurrent EEG recording. Motor learning investigations of tDCS typically apply large rectangular electrodes centered over C3 (Reis et al., 2009; Buch et al., 2017). Because such an electrode would hinder quality EEG recording, we opted to use small circular (~1 cm diameter) electrodes used for high-definition tDCS (Soterix Medical Inc., New York City, USA). Transcranial stimulation was applied per published standards (Woods et al., 2016) by an experienced investigator. The anode was positioned on the dominant hemisphere at CP3 or CP4. Four cathodes were placed on the contralateral hemisphere, surrounding F3 or F4. Four cathodes were used to disperse the current over the frontal cortex rather than having a focal intensity of current. A high viscosity electrolyte-gel was placed under the electrodes to form a bridge to the scalp surface. Computational modeling using SimNIBS suggests that this modified montage may generate stronger electric fields in the precentral sulcus, compared to conventional tDCS montages (Supplementary Fig. S1), but overall induces similar electric field patterns. SimNIBS electric field modeling is described elsewhere (Windhoff et al., 2013). Electrodes were connected to a 4x1 Adaptor (Soterix Medical Inc.) coupled to a 1x1 tDCS unit (Soterix Medical Inc.).

Stimulation was initiated following completion of the baseline pattern cutting and peg transfer. In both sham and anodal tDCS the current was ramped to 1 mA over 30 s. In the sham condition the current immediately ramped down to 0 mA, whereas in the anodal condition the current strength remained at 1 mA for 20 min. This sham procedures generates similar sensations to those as anodal tDCS, however does not induce lasting changes in cortical excitability (Ambrus et al., 2012).

4.8. Sample size

Power analysis was conducted using SigmaPlot (ver. 12.5; Systat Software Inc., San Jose, USA). Sample size calculation was based on our previous study of the effects of tDCS on laparoscopic skill acquisition (Ciechanski et al., 2018), specifically, interventional effects on change in pattern cutting score at the post-training time point. Based on a 15% greater improvement of FLS pattern cutting score with anodal tDCS compared to sham, and combined with a $\sigma = 10.0$, $\alpha = 0.05$, and power of 90%, an independent samples *t*-test power calculation estimated that a total of 10 participants per intervention group would be required.

4.9. Statistical analysis

Statistical analysis was performed using SPSS (ver. 23; IBM, Armonk, USA). Baseline demographics and characteristics were compared between intervention groups using independent samples t-tests or Chi-square/Fisher exact test. Correlations between population characteristics and baseline performance were explored using Pearson's correlation. Pattern cutting and peg transfer learning curves were compared using two-way mixed-design analysis of variance (rmANOVA) examining factors of TIME and INTERVENTION. Post-training pattern cutting and peg transfer scores were compared across groups using independent samples t-tests. Subsequently, participants were categorized as low- or high-skill performers, delineated by the median pattern cutting and peg transfer scores of the entire sample, as described elsewhere yy (Ciechanski et al., 2017). Intervention effects on task performance were examined in low- and high-skill participants using a Mann-Whitney *U* test on post-training scores (to account for sample size). Comparison of changes in EEG power from baseline to post-training in the sham condition, suggesting of effects of training alone, were analyzed using rmANOVA examining factors of ELECTRODE LOCATION and TIME and TASK. Bonferroni's adjustment for multiple comparisons was applied. Baseline EEG recordings of pattern cutting and peg transfer skill were analyzed using rmANOVA examining factors of ELECTRODE LOCATION and TASK. Bonferroni's adjustment for multiple comparisons was applied. Multivariate ANOVA (MANOVA) examined intervention effects on change in frequency band power between baseline and post-training performance. A separate MANOVA, with dependent factors consisting of each frequency band, was performed for pattern cutting and peg transfer tasks. To examine correlations between change in pattern cutting or peg transfer score and change in frequency band power we performed Pearson's correlation with a Benjamini-Hochberg procedure to correct for multiple comparisons. A false-detection rate of 0.05 was used for the Benjamini-Hochberg procedure, a conservative value. For all t-tests Levene's Test for Equality of Variance was applied, and appropriate statistics reported. For all ANOVA, Mauchley's Test of Sphericity was run, and when the assumption of sphericity was violated the Greenhouse-Geisser correction was used. To examine differences in the proportion of participants reporting sensations associated with tDCS we performed a Chi-square test. To examine differences in the severity of these sensations we performed independent samples t-tests. Statistical significance was stated when $p < 0.05$. When applicable, values display mean ± standard deviation.

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Declaration of Competing Interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brainres.2019.146445.

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