Supplementary motor area contributions to rhythm perception

Authors: Li-Ann Leow[1], Cricia Rinchon[2], Marina Emerick[3], Jessica A. Grahn[3,4]

[1] School of Psychology, The University of Queensland, Australia

[2] Institute of Medical Science, University of Toronto, Canada

[3] The Brain and Mind Institute, Western University, Canada

[4] Department of Psychology, Western University, Canada

Keywords: Rhythm; music; timing; neuroscience, transcranial direct current stimulation.

Abstract

Timing is everything, but our understanding of the neural mechanisms of timing remains limited, particularly for timing of sequences. Temporal sequences can be represented relative to a recurrent beat (beat-based or relative timing), or as a series of absolute durations (non-beat-based or absolute timing). Neuroimaging work suggests involvement of the basal ganglia, supplementary motor area (SMA), the premotor cortices, and the cerebellum in both beat- and non-beat-based timing. Here we examined how beat-based timing and non-beat-based sequence timing were affected by modulating excitability of the supplementary motor area, the right cerebellum, and the bilateral dorsal premotor cortices, using transcranial direct current stimulation (tDCS). Participants were subjected to a sham stimulation session, followed an active stimulation session where anodal or cathodal 2mA tDCS was applied to the SMA, right premotor cortex, left premotor cortex, or the cerebellum. During both sessions, participants discriminated changes in rhythms which differentially engage beat-based or non-beat-based timing. Rhythm discrimination performance was improved by increasing SMA excitability, and impaired by decreasing SMA excitability. This polarity-dependent effect on rhythm discrimination was absent for cerebellar or premotor cortex stimulation, suggesting a crucial role of the SMA and/or its functionally connected networks in rhythmic timing mechanisms.

A fascinating, possibly uniquely human behaviour is the capacity to perceive the beat in sequences of temporal intervals (e.g., in music or speech), even though beats are not necessarily indicated by distinguishing acoustic features. Beat perception, or the ability to sense a beat in rhythms, appears spontaneously in humans, without training (Winkler et al., 2009). Beat perception is thought to engage relative timing mechanisms, in which the temporal intervals of a pattern are coded relative to each other (Essens & Povel, 1985; Yee *et al.*, 1994; Teki *et al.*, 2011a; Teki *et al.*, 2011b). This relative timing is often called 'beat-based' timing, because the intervals can be encoded relative to a regular, periodic beat interval. Beat-based timing improves accuracy during discrimination, synchronization, and reproduction of temporal sequences (Essens & Povel, 1985; Yee *et al.*, 1994; Patel *et al.*, 2005; Grahn & Brett, 2007; Chen *et al.*, 2008c). Relative timing stands in contrast to 'absolute' timing, also termed duration-based or non-beat-based timing, in which the absolute durations of temporal intervals are encoded individually in a stop-watch like manner (Teki *et al.*, 2011a).

An large body of functional neuroimaging studies have suggested involvement of the supplementary motor area (SMA), the basal ganglia, the premotor cortex, and the cerebellum in timing (e.g., Schubotz & von Cramon, 2001; Ullen *et al.*, 2003; Lewis *et al.*, 2004; Grahn & Brett, 2007; Chen *et al.*, 2008b; Bengtsson *et al.*, 2009; Teki *et al.*, 2011b). Determining the specific role of each area in different timing processes remains an active area of investigation. Neuroimaging studies find that the SMA and basal ganglia respond more to beat-based than non-beat-based than rhythms (Grahn & Brett, 2007; Grahn & Rowe, 2009; Teki *et al.*, 2011b; Geiser *et al.*, 2012; Grahn & Rowe, 2013; Li *et al.*, 2019). This pattern is consistent across tasks, including perceptual judgements (McAuley *et al.*, 2012), discrimination (Grahn & Brett, 2007), or attending to non-temporal aspects of the stimuli such as loudness (Geiser, Notter, & Gabrieli, 2012) and pitch (Grahn & Rowe, 2009). Moreover, neuropsychological work in patients with Parkinson's disease finds selective deficits in beat-based, but not non-beat-based timing (Grahn & Brett, 2009; Breska & Ivry, 2018). The premotor cortex and cerebellum appear to respond in both beat-based and non-beat-based contexts (Bengtsson *et al.*, 2005; Chen *et al.*, 2006), or respond more to non-beat-based than to beat-based contexts (Grahn & Rowe, 2009; Nozaradan et al., 2017; Teki et al., 2012). In a similar vein, patients with cerebellar degeneration show selective deficits in non-beat-based timing, despite showing intact beat-based timing (Grube et al., 2010a; Breska & Ivry, 2018). It has thus been suggested that a functional network involving the SMA and basal ganglia subserves beat-based timing, whereas a functional network involving the cerebellum subserves absolute timing (e.g., Teki *et al.*, 2011b).

Importantly however, the theory of distinct neural processes subserving beat-based and non-beat based timing has mostly been supported by correlational neuroimaging evidence(Grahn & Brett, 2007; Grahn & Rowe, 2009; Teki *et al.*, 2011b; Geiser *et al.*, 2012; Grahn & Rowe, 2013; Li *et al.*,

2019), or by neuropsychological work in patient populations (Grahn & Brett, 2009; Grube *et al.*, 2010a; Breska & Ivry, 2018) who can have more global deficits that might not relate directly to the task. Relatively few studies employ perturbational methods in neurotypical humans, and such studies typically perturb only one or two brain areas implicated in beat perception (Malcolm *et al.*, 2008; Grube *et al.*, 2010b; Giovannelli *et al.*, 2014; Ross *et al.*, 2018b). Here, in neurotypical young adults, we examine how beat perception is affected by modulating multiple brain areas implicated in beat-based and non beat-based timing (i.e., supplementary motor area, left and right premotor cortex, and cerebellum), using transcranial direct current stimulation. Transcranial direct current stimulation (tDCS) is thought to modulate spontaneous neural firing and synaptic efficacy of neurons by altering resting membrane potential (e.g., Bindman *et al.*, 1962; Lafon *et al.*, 2017), and has been proposed to have functionally specific effects by modulating activity of task-relevant neuronal networks (Bikson & Rahman, 2013). Given the large individual differences in beat perception ability (Grahn & McAuley, 2009; Grahn & Schuit, 2012; Sowinski & Dalla Bella, 2013), as well as large individual differences in tDCS responsivity (Chew *et al.*, 2015), we employed a within-subjects approach, where participants completed a placebo (sham) tDCS session followed by an active tDCS session whilst discriminating between rhythms which differentially engage beat-based timing. We hypothesize that a functional network involving the SMA plays a primary role in beat-based timing: thus, modulating excitability of the SMA was predicted to affect performance when processing beat-inducing rhythms.

Method

Participants

A total of 121 participants completed the experiment for course credit. Cerebellum anodal (n=14), cerebellum cathodal (n=16), left premotor anodal (n=15), left premotor cathodal (n=16), right premotor anodal (n=15) right premotor cathodal (n=15), SMA anodal (n=15), SMA cathodal (n=15). Participants were not pre-selected for music or dance training. Participants passed a safety screening for tDCS and gave informed consent. The Human Research Ethics Committee at Western University approved the study and all experiments were performed in accordance with relevant guidelines and regulations.

Transcranial Direct Current Stimulation

Transcranial direct current stimulation (tDCS) involves passing a weak current from one area of the brain to another area of the brain. Unlike transcranial electric and transcranial magnetic current stimulation, tDCS does not itself cause neural firing: it modulates spontaneous firing and synaptic efficacy of neurons by altering resting membrane potential. Anodal tDCS increases the likelihood of spontaneous neural firing, whereas cathodal tDCS decreases the likelihood of spontaneous neural

firing (Purpura & McMurtry, 1965). tDCS thus modulates neuronal networks activated at the time Hence, despite its lack of spatial specificity, tDCS can be functionally specific (Bikson & Rahman, 2013).

Before behavioural testing, the scalp area overlying the stimulation site was located using the international electroencephalographic 10-20 system. This method of localization is sufficient for tDCS using large electrodes as used here (Fregni *et al.*, 2006). Electrode montages are as follows. **SMA**: active electrode positioned 2 cm anterior to Cz, reference electrode positioned on contralateral orbit (Vollmann *et al.*, 2013). **Cerebellum**: active electrode positioned 3 cm right of the inion, reference electrode positioned on the right buccinator muscle (Galea *et al.*, 2009). **PMC**: active electrode positioned 2 cm anterior and 2 cm to the right of C3 for left PMC, and 2cm anterior and 2cm to the right of C4 for right PMC (Nitsche *et al.*, 2003; Boros *et al.*, 2008), as neuroimaging studies suggest that the dorsal premotor cortex is located about 15–25 mm anterior to the primary motor cortex (C3, C4)(Picard & Strick, 2001). The reference electrode was positioned on contralateral orbit for both right and left PMC. Electrodes were secured using Velcro straps. For the active tDCS conditions, the current was gradually ramped up to the 2 mA level over 30 s upon commencing the rhythm discrimination task. The stimulation remained on during the task for a maximum of 40 minutes and was ramped down at the end of the stimulation period. For the sham tDCS conditions, the stimulation was ramped off over 30 s immediately after reaching 2 mA. This method is sufficient to achieve blinding in stimulation-naïve participants (Ambrus *et al.*, 2012). Stimulation was generated with a Dupel Stimulator (Dupel Ionophoresis System, MN) using two 4 x 6 cm rubber electrodes placed in saline-soaked sponges (current density of 0.04 mA/cm2; 0.9% NaCl) and highly conductive electrode gel (e.g., Signa Gel 40,000 micromhos/cm).

We employed a within-subjects approach to counter the large individual differences in beat perception ability (Grahn & McAuley, 2009; Grahn & Schuit, 2012; Sowinski & Dalla Bella, 2013), as well as large individual differences in tDCS responsivity (Chew *et al.*, 2015). Each participant first completed a first sham tDCS condition in a first session, followed by active tDCS in the second session. In each session, during stimulation, participants completed the rhythm discrimination task (described below), with different rhythms used for each session to reduce practice effects. Participants completed both sessions on one visit, allowing us to eliminate participant drop-outs between visits. Time constraints made it unfeasible to have the active tDCS condition before the sham tDCS condition within a single-visit design, as effects can persist up to an hour post-stimulation (Nitsche & Paulus, 2000): waiting for tDCS effects to washout would require the visit to last more than 3 hours.

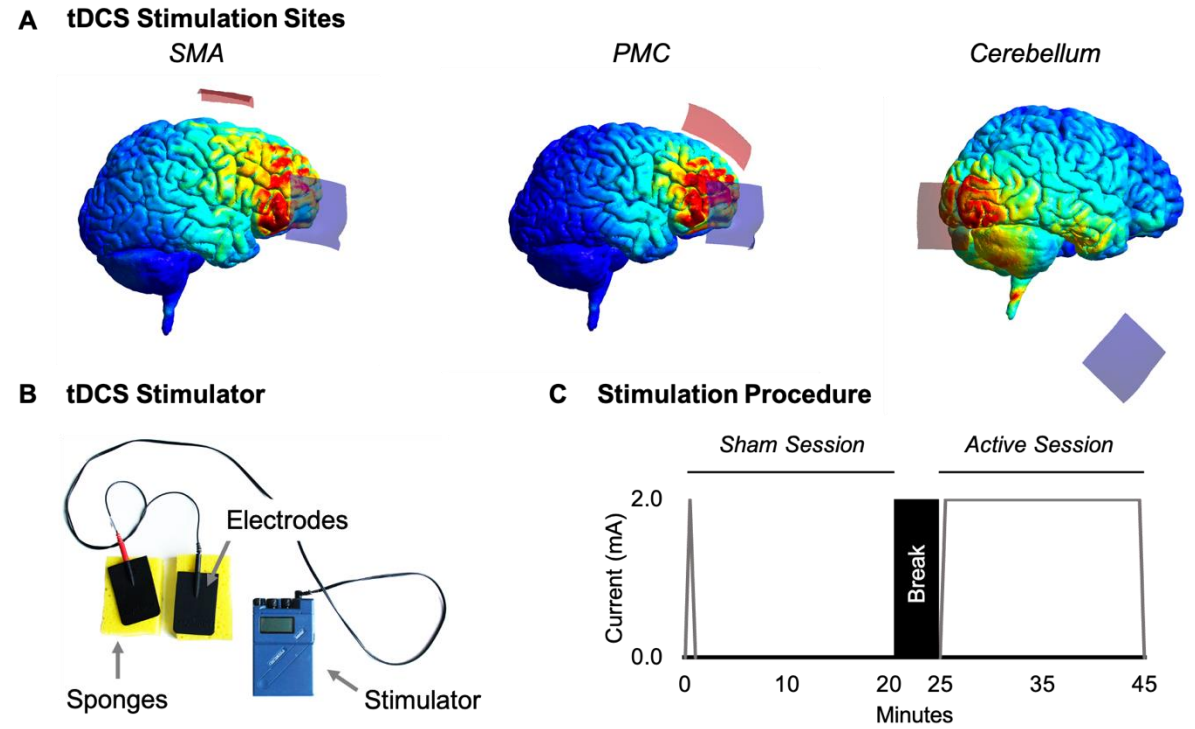

Figure 1. (A) Stimulation sites and simulated electric field distributions. SimNIBS was used to calculate current flow calculations and generate images of simulated electric field distributions. Active electrode positions: **SMA:** 2 cm anterior to Cz. **PMC:** active electrode 2 cm medial to C3 for right PMC, 2cm medial to C4 for left PMC. **Cerebellum:** 2 cm right of the inion. Reference electrode positions: contralateral orbit for all conditions except cerebellum (right buccinator muscle. **(B) tDCS Stimulator:** Dupel Ionophoresis System, two 4 x 6 cm rubber electrodes placed in saline-soaked sponges, and conductive electrode gel. **(C) Stimulation Procedure:** 20-minutes of sham stimulation followed by 20-minutes of active tDCS. For the sham tDCS conditions, the stimulation was ramped up over 30 seconds, and then ramped down to 0 over 30 s immediately after reaching 2 mA. For the active tDCS conditions, the current was gradually ramped up to 2 mA over 30 seconds upon commencing the rhythm discrimination task.

Auditory Stimuli. We used rhythms which differentially induces beat perception as in previous work (Grahn & Brett, 2007). These rhythms were created using integer ratio intervals, which were related by ratios of 1:2:3:4. For **metric simple rhythms** (i.e., **beat-inducing rhythms**), the intervals were arranged in groups of four units (e.g., in the sequence 211314, an interval onset consistently occurs every four units). The patterns were constructed to induce a regular perceptual accent at the beginning of each group of four units (Povel & Okkerman, 1981). For **metric complex rhythms** (i.e., **non-beat-inducing rhythms**), the intervals were re-arranged, such that they tend not be reliably grouped into two, three, or four units (e.g., 341211). Since there is no regular grouping, there is no regular perceptual accent.

For both rhythm types, the shortest interval (i.e., 1) ranged from 220 to 270 ms, in 10 ms steps. Sine tones (rise/fall times of 8 ms) sounded for the duration of each interval, ending 40 ms before the specified interval length to create a silent gap that demarcated the intervals. The sequences used filled intervals, as opposed to a brief presentation of the stimulus marking interval onset). The other intervals in the rhythm were multiples of the shortest interval. The perceptual accents cued

participants to a regular beat structure, in which the beats coincided with the onset of each group (Essens, 1995). In addition, if participants choose a faster rate for the beat, the sequence can still be measured by that rate (e.g., measured in units of two rather than four).

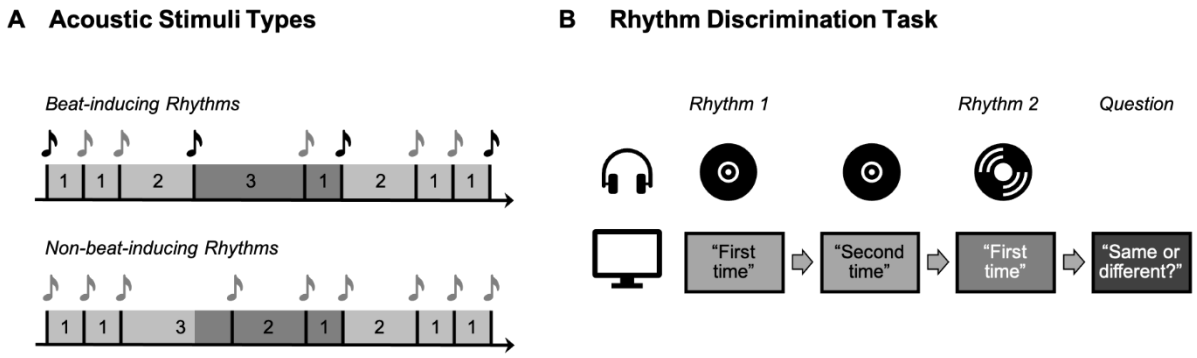

Figure 2. (**A) Acoustic stimuli types:** schematic example of the two types of rhythmic sequence stimuli used. Numbers denote the length of intervals in each sequence. 1 = 220-270 ms. Beat-inducing rhythms (also termed metric simple rhythms) had intervals that could be grouped regularly (i.e., 1, 1, 2 could be grouped, as 3,1 and 2,1,1, could be grouped regularly*)* inducing a perceptual beat. Non-beat-inducing rhythms (also termed metric complex rhythms) could not be grouped regularly. **(B) Rhythm Discrimination Task:** participants were asked to listen to a first rhythm twice, and then a second rhythm. Participants were asked to decide if the third rhythm was the same or different from the first rhythm.

Table 1. Rhythm Discrimination Task – Rhythm Sequences

Beat-Inducing (i.e., metric simple rhythms)		Non-Beat-Inducing (i.e., metric complex rhythms)	
Standard	Deviant	Standard	Deviant
1111431	1111413	1112412	1112142
1122114	1121124	1132131	1123212
1123113	1121322	1132212	1311411
1123122	112224	11343	13143
112314	112224	121233	1411221
112422	1123131	122142	14133
211134	211314	124113	2313111
2112231	2113131	1314111	2321112
211224	211314	132321	23214
2113113	211431	13242	23214
211413	223131	13242	241221
2211114	312231	1411311	241311
221331	313122	2123211	3131121
222114	4111113	2141211	31341
223113	41322	214221	322311
22413	4211211	214311	324111
311322	43131	221241	
3121113		231123	
3122112		23241	
312213		23241	
3141111		2331111	
31413		3113121	
31422		3114111	
4111131		321411	
411231		3221112	
41331		323211	
4221111		33141	
422112		4111221	
43113		41133	
43122		412212	
		41232	
		41232	
		421311	

1 = 220—270 msec (in steps of 10 msec), chosen at random for each trial. All other intervals in that sequence are multiplied by length chosen for the 1 interval. Modified from Grahn & Brett (2009).

Task Procedure

Rhythms were presented binaurally over Sennheiser headphones. Participants first completed four familiarization trials, where they were asked to judge whether the third presentation of a rhythm was the same as or different from the first two presentations. Participants completed the first session of 30 trials whilst undergoing sham stimulation, followed by a second session of 30 trials whilst undergoing active stimulation.

In each trial, a rhythm was presented three times. Participants compared the third presentation of a rhythm to the first two presentations. The words 'First time', 'Second time', and 'Same or different?' were displayed on the screen during the first, second, and third rhythm presentations, respectively. Participants indicated their response by pressing one key for 'same' and another key for 'different' on a computer keyboard. Between trials, there was a 2s interval of silence. On half of the trials, the rhythm in the third presentation deviated from the first two presentations. The deviant sequences contained a transposition of intervals in the sequence (see Table 1). For example, the sequence 211413 can have as a possible deviant sequence 211431, in which the 3 interval and the 1 interval have been transposed. Only deviant sequences that were in the same category as the standard sequences were allowed. That is, a metric simple standard sequence could not have a metric complex deviant sequence, and a metric complex standard sequence could not have a metric simple deviant sequence.

Data Analysis

Task performance was quantified using sensitivity (*d'* scores) and percent correct scores, consistent with previous work (Grahn & Brett, 2007).

Statistical analysis

Unlike p-values, Bayes factors do not tend to over-estimate the evidence against the null hypothesis (Gelman & Tuerlinckx, 2000; Wetzels *et al.*, 2011). We thus chose to use Bayesian statistics to evaluate evidence for the alternative hypothesis and for the null hypothesis. Analyses were conducted in JASP (Version 0.13.1; JASP Team, 2020). The default Cauchy prior widths (0.707) values in JASP were used to quantify the relative evidence that the data came from the alternative versus a null model.

To evaluate stimulation-induced changes in discrimination performance across different stimulation sites and polarities, Rhythm (metric complex, metric simple) x Stimulation (sham, stimulation) x Polarity (anodal, cathodal) x Site (SMA, cerebellum, right PMC, left PMC) bayesian ANOVAs were run on *d'* and percent correct. Analyses estimated the evidence for including each

effect across matched models via estimating inclusion Bayes factor (BF_{incl}) for each effect. Analyses also estimated the evidence for excluding each effect by estimating an exclusion Bayes factor (BF_{excl}) for each effect. Where applicable, simple effects analyses were used to follow-up interactions. Jeffreys's evidence categories for interpretation, were taken as the standard for evaluation of the reported Bayes Factors, where the size of the Bayes factors were estimated as weak (1–3), substantial (3–10), or strong (>10) evidence for the hypotheses tested.

Results

Effect of tDCS on rhythm discrimination

Rhythm discrimination performance

Replicating previous results (Grahn & Brett, 2009; Grahn, 2012), *d'* and percent correct scores were higher for metric simple than for metric complex rhythms, indicating better discrimination performance for metric simple rhythms than for metric complex rhythms [*d'*: metric complex: 1.16±0.06, metric simple: 1.76±0.08; percent correct: metric complex= 69.1±0.9%, metric simple= 76.6±1.1%; main effect of rhythm type BF_{incl} = 6.267e+28]. Figure 3 and 4 respectively show *d'* and percent correct scores and from the sham condition to the stimulation condition. Generally, patterns in percent correct scores appear similar to *d'* scores, similar to previous work (Grahn & Brett, 2007; 2009).

Stimulation affected rhythm discrimination performance differently depending on stimulation site and stimulation polarity, as shown by Stimulation x Site x Polarity interactions [*d'*: BF_{incl} = 3.019, percent correct: BF_{incl} = 2.574]. Follow-up Rhythm (metric complex, metric simple) x Stimulation (Sham, Stimulation) x Polarity (Anodal, Cathodal) were run separately for each stimulation site.

For SMA, there were Stimulation (Sham, Anodal) x Polarity (Anodal, Cathodal) interactions [*d'*: BF_{incl} = 298.500, percent correct: BF_{incl} = 288.447]. Follow-up simple effects analyses (i.e., Rhythm x Stimulation Bayesian ANOVAs) run separately for the anodal and cathodal conditions showed that anodal SMA stimulation improved discrimination performance compared to sham, particularly for metric simple rhythms (main effect of stimulation for *d'*: BF_{incl} = 4.060, percent correct: BF_{incl} = 3.679 (see Figure 3 and 4), whereas cathodal SMA stimulation worsened discrimination performance compared to sham (main effect of stimulation for *d'*: BF_{incl} = 16.732, percent correct: BF_{incl} =17.243).

For cerebellum, there was some evidence suggesting that stimulation worsened discrimination performance, [*d'*: BF_{incl} = 1.941, percent correct: BF_{incl} = 9.102], which appeared

polarity-independent (substantial evidence against the stimulation by polarity interaction [*d'*: BF_{excl} = 3.710, percent correct: BF_{excl} = 2.985].

For the left premotor cortex condition, stimulation appeared to have no effect, as there was substantial evidence against including the main effect of stimulation [*d':* BF_{excl} = 5.175; percent correct: BF_{excl} = 4.466] and the stimulation x polarity interaction [*d'*: BF_{excl} = 3.614, percent correct: BF_{excl} = 3.913]. Similarly for the right premotor cortex condition, there was evidence to exclude the main effect of stimulation [*d':* BF_{excl} = 2.315; percent correct: BF_{excl} = 7.347e -8] and the stimulation x polarity interaction [*d':* BF_{excl} = 3.592, percent correct: BF_{excl} = 3.713].

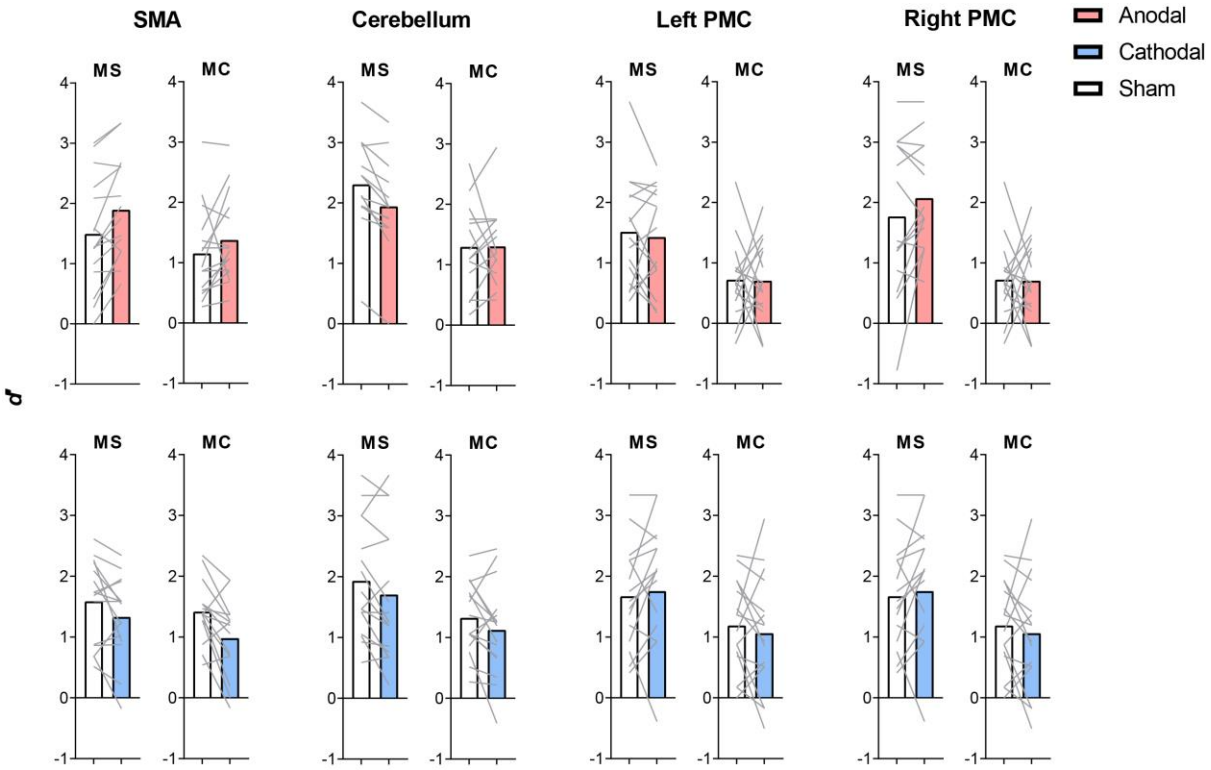

Figure 3. *d'* from the sham stimulation session (white bars) and the active stimulation session (coloured bars, where pink indicates anodal tDCS whereas blue indicates cathodal tDCS), with metric simple (MS) and metric complex (MC) rhythms.

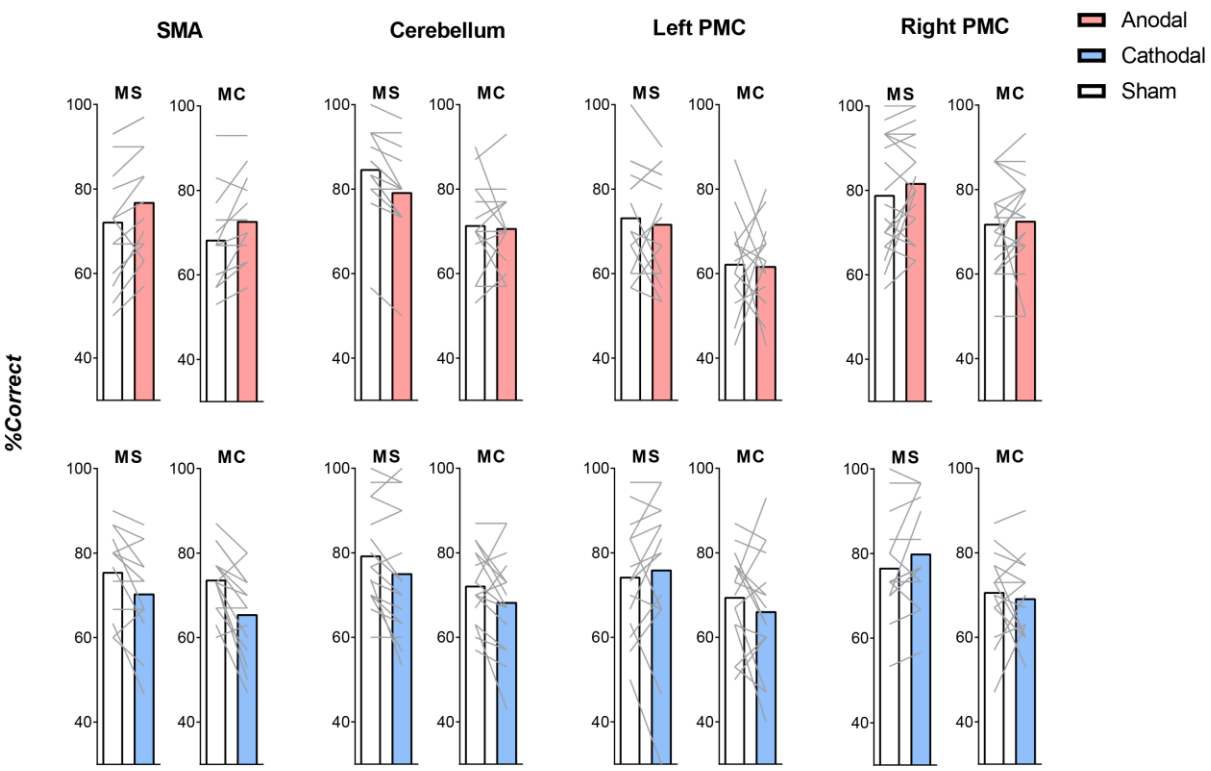

Figure 4. Response accuracy from the sham stimulation session (white bars) to the active stimulation session (coloured bars, where pink indicates anodal tDCS whereas blue indicates cathodal tDCS), as indicated by percent of trials correct for anodal (top panels) and cathodal (bottom panels) tDCS conditions, with metric simple (MS) and metric complex (MC) rhythms.

Discussion

Here, we provide initial evidence suggesting that discrimination of metric simple and metric complex rhythms can be improved by increasing SMA excitability, and impaired by decreasing SMA excitability. This polarity-dependent effect on discrimination of metric simple rhythms was not evident for cerebellar or premotor cortex stimulation, suggesting a functional role of the SMA and/or its functionally connected networks in beat-based timing.

How might the SMA support beat-perception?

Here, we found that modulating SMA excitability altered performance on the rhythm discrimination task in a polarity-dependent fashion. These findings support the idea that the SMA and the basal ganglia are involved in maintaining an internal representation of beat intervals (Grahn & Brett, 2007; Grahn & Rowe, 2009), facilitating performance on the rhythm discrimination task. Our results are broadly consistent with findings of greater SMA-basal ganglia activation during the processing of metric simple rhythms compared to metric complex rhythms (Grahn & Brett, 2007; Grahn & Rowe, 2009). It has been suggested that the SMA networks help to form forward temporal predictions (Macar *et al.*, 2004). The role of the SMA in beat-maintenance is consistent with evidence

in synchronization-continuation tasks where participants are asked to synchronize movements to external stimuli and then continue synchronization upon withdrawal of the external stimuli: here, the SMA tends to be activated during the continuation phase, and not the synchronization phase (Rao *et al.*, 1997; Lewis *et al.*, 2004). Similarly, patients with SMA lesions also show a selective deficit in the continuation phase but not the synchronization phase of the synchronization-continuation task (Halsband *et al.*, 1993). Recent proposals have suggested that the SMA is tuned to anticipate an upcoming beat interval, and sends signals to the dorsal striatum, helping the striatum generate internally generated representations of the beat cycle, which in turn activates new SMA neural subpopulations via the thalamus (Cannon & Patel, 2021). Future studies might test this hypothesis via recordings in SMA and basal ganglia, perhaps in patients with electrocorticography and deep brain stimulator implants.

Effect of premotor cortex tDCS on rhythm discrimination performance

The premotor cortex is thought to be engaged in planning, selection, and control motor programs based on external events (Picard & Strick, 2001). The finding that stimulation of the left or right premotor cortex did not interfere with rhythm discrimination performance is consistent with the idea that the premotor cortex plays a primary role in synchronization and control of motor programs in response to external events, rather than beat perception per se. Although some findings implicate a role of the premotor cortex in beat-based timing (Chen *et al.*, 2006; Chen *et al.*, 2008a; c; 2009), all of these studies involve the synchronization of rhythms using repetitive TMS. Synchronization requires participants to synchronize movements to the onset of each tone of a rhythm, or to each beat in the rhythm. This not only requires participants to encode and maintain the beat interval, but also to produce a synchronized motor response, evaluate the accuracy of that response after each tap, and correct the timing of inaccurate taps. Indeed, the greater difficulty of synchronizing to non-beat rhythms (and consequently greater demands on motor planning, evaluation, and error correction) might have resulted in the increased premotor cortex activation when synchronizing to non-beat-rhythms than beat rhythms (Chen *et al.*, 2008c). The notion that the premotor cortex plays a general role in synchronization of movements to external stimuli is supported by an increasing body of evidence showing that non-invasive stimulation of the premotor cortex modulates synchronization performance, when synchronizing to isochronous cues (Doumas *et al.*, 2005; Del Olmo *et al.*, 2007; Malcolm *et al.*, 2008; Pollok *et al.*, 2008; Bijsterbosch *et al.*, 2011; Ruspantini *et al.*, 2011), when adjusting for changes in cue onsets (Bijsterbosch *et al.*, 2011; Kornysheva & Schubotz, 2011a; Ruspantini *et al.*, 2011), or when tapping to rhythms which differentially engage beat perception (Kornysheva & Schubotz, 2011b; Giovannelli *et al.*, 2014). These findings show distinct effects of stimulation on aspects of synchronization (e.g., tempo-matching versus phase-matching), and different effects on dorsal versus ventral premotor cortex stimulation, or left versus right premotor

cortex stimulation. A detailed discussion of these findings is outside the scope of this study. To the best of our knowledge, there are no papers published in peer-reviewed journals demonstrating effects of stimulating the premotor cortex on beat perception tasks that do not require motor synchronization to external stimuli in humans. One study currently published on a preprint server has examined how stimulation of premotor cortex affects capacity to perceive changes in tempo in music (Ross *et al.*, 2018a). However, music contains many redundant cues that signal beat onsets which aid the perception of tempo changes: effects of premotor cortex stimulation in this study might thus not be directly related to beat perception in temporal intervals without redundant cues. To elucidate the role of the premotor cortex in perceiving and synchronizing to the beat, future studies should examine effects of modulating premotor cortex excitability on the processing of beat and non-beat-based rhythms using both perceptual tasks and motor synchronization within the same subjects.

Effect of cerebellar tDCS on rhythm discrimination performance

Cerebellar tDCS resulted in lower discrimination accuracy (i.e., percent correct scores) regardless of stimulation polarity, with both beat and non-beat rhythms, although this effect appeared more robust for percent accuracy than discrimination sensitivity (*d')*. The polarity-independent effect on discrimination accuracy is perhaps unsurprising given the increasing numbers of studies that show polarity-independent effects of anodal and cathodal cerebellar tDCS on working memory (Ferrucci et al., 2008; Van Wessel et al., 2016), motor control and learning (Shah et al., 2013; Verhage et al., 2017), motor memory retention (Taubert et al., 2016), and conditioned eyeblink responses (Beyer et al., 2017). Indeed, one recent meta-analysis found no evidence for a polarity-dependent effect of cerebellar tDCS (Oldrati & Schutter, 2018). Polarity-dependent effects of tDCS on cortex do not necessarily generalize to the cerebellum, as the organization of cerebellar neurons differs fundamentally from that of the cortex (van Dun et al., 2016; Woods et al., 2016).

A few interpretations are possible for how cerebellar tDCS impaired discrimination accuracy here. First, cerebellar tDCS might have induced impairments in working memory, similar to previous findings (Van Wessel et al., 2016)(Ferrucci et al., 2008). In the rhythm discrimination task used here, working memory is required to remember and compare the first rhythms with the test rhythms. Second, cerebellar tDCS might have impaired absolute timing processes, consistent with previous findings of worsened absolute timing (Grube *et al.*, 2010b). Both interpretations may be true. Judicious experimental designs which explicitly manipulate working memory load and/or stimuli which differentially engage absolute timing might provide evidence for or against these two possible interpretations.

Limitations

An important limitation in the current work is the lack of counterbalancing of the order of sham and active tDCS: the sham tDCS session always preceded the active tDCS session. Thus, the results of tDCS shown here might be interpreted as affecting *learning* to discriminate rhythms rather than performance in discriminating rhythms. Importantly however, only the group receiving anodal SMA tDCS improved rhythm discrimination performance from the first sham tDCS session to the second active tDCS session. No improvement in discrimination performance was evident in any other group. A general learning effect could only be true if stimulation for all the other sites (left PMC, right PMC, cerebellum) modifies the learning effect. Furthermore, the cathodal SMA tDCS group also showed worse rhythm discrimination in their second active tDCS session than in their first sham tDCS session. Furthermore, previous studies which test the effect of SMA stimulation do not show effects of SMA tDCS on learning (Foerster *et al.*, 2013). It thus seems more likely that SMA tDCS modulated capacity to discriminate rhythms, rather than *learning* to discriminate rhythms.

A second limitation is the difficulty in blinding tDCS administration. Blinding in tDCS can be challenging even using double-blind designs where one experimenter conducts electrode placement and initiates stimulation and a different experimenter administers the behavioural task (O'connell *et al.*, 2012). Here we used a single-blind design, and did not assess participant or experimenter blinding. Our protocols of employing sham tDCS first followed by active tDCS could have unblinded participants (Turi *et al.*, 2019). Participants however, likely remained blinded to stimulation polarity, and it seems unlikely that participant expectations could have resulted in polarity-dependent effect of stimulation the SMA. We also did not predict the effect of cerebellar tDCS impairing rhythm discrimination performance regardless of stimulation polarity: this effect seems unlikely to have resulted from participant or experimenter expectations. Finally, the selective polarity-dependent effect on SMA but not for right and nor left premotor cortex conditions suggests a genuine effect of SMA stimulation on rhythm discrimination performance. However, it is clear that tDCS effects can be variable between individuals (Chew *et al.*, 2015) as well as within individuals (e.g., Chew *et al.*, 2015; López-Alonso *et al.*, 2015), with factors such as cortical morphology (e.g.,Filmer *et al.*, 2020), neurochemical concentrations (e.g., Filmer *et al.*, 2020), genetics, time of day, gender, age, hormone levels (for a review, see Ridding & Ziemann, 2010). This work presents initial evidence suggesting that SMA tDCS can modulate rhythm discrimination performance. Replication and extension of this work will be necessary to increase confidence in these results.

Summary

Neuroimaging and neuropsychological evidence implicate a role of a functional network encompassing the supplementary motor area and the putamen in beat perception. Here, we show that

non-invasive stimulation of the supplementary motor area can have polarity-dependent effects on discrimination of auditory rhythm. Although the current evidence implicates a role of the supplementary motor area in beat perception, exactly how the SMA interacts with other brain areas during beat perception remains unclear. Exploring this question by combining perturbational methods such as brain stimulation with methods that afford both high temporal and spatial resolution (e.g., magnetoencephalography) could elucidate the mechanisms through which regions implicated in processing time interact and contribute to beat perception.

References

Ambrus, G.G., Al-Moyed, H., Chaieb, L., Sarp, L., Antal, A. & Paulus, W. (2012) The fade-in--short stimulation--fade out approach to sham tDCS--reliable at 1 mA for naive and experienced subjects, but not investigators. *Brain Stimul*, **5**, 499-504.

Bengtsson, S.L., Ehrsson, H.H., Forssberg, H. & Ullen, F. (2005) Effector-independent voluntary timing: behavioural and neuroimaging evidence. *Eur J Neurosci*, **22**, 3255-3265.

Bengtsson, S.L., Ullén, F., Henrik Ehrsson, H., Hashimoto, T., Kito, T., Naito, E., Forssberg, H. & Sadato, N. (2009) Listening to rhythms activates motor and premotor cortices. *Cortex*, **45**, 62-71.

Bijsterbosch, J.D., Lee, K.H., Dyson-Sutton, W., Barker, A.T. & Woodruff, P.W. (2011) Continuous theta burst stimulation over the left pre-motor cortex affects sensorimotor timing accuracy and supraliminal error correction. *Brain Res*, **1410**, 101-111.

Bikson, M. & Rahman, A. (2013) Origins of specificity during tDCS: Anatomical, activity-selective, and input-bias mechanisms. *Frontiers in Human Neuroscience*.

Bindman, L.J., Lippold, O. & Redfearn, J. (1962) Long-lasting changes in the level of the electrical activity of the cerebral cortex produced by polarizing currents. *Nature*, **196**, 584-585.

Boros, K., Poreisz, C., Münchau, A., Paulus, W. & Nitsche, M.A. (2008) Premotor transcranial direct current stimulation (tDCS) affects primary motor excitability in humans. *European Journal of Neuroscience*, **27**, 1292-1300.

Breska, A. & Ivry, R.B. (2018) Double dissociation of single-interval and rhythmic temporal prediction in cerebellar degeneration and Parkinson's disease. *Proc Natl Acad Sci U S A*, **115**, 12283-12288.

Cannon, J.J. & Patel, A.D. (2021) How Beat Perception Co-opts Motor Neurophysiology. *Trends Cogn Sci*, **25**, 137-150.

Chen, J.L., Penhune, V.B. & Zatorre, R.J. (2008a) Listening to musical rhythms recruits motor regions of the brain. *Cereb Cortex*, **18**, 2844-2854.

Chen, J.L., Penhune, V.B. & Zatorre, R.J. (2008b) Listening to Musical Rhythms Recruits Motor Regions of the Brain. *Cerebral Cortex*, **18**, 2844-2854.

Chen, J.L., Penhune, V.B. & Zatorre, R.J. (2008c) Moving on time: brain network for auditory-motor synchronization is modulated by rhythm complexity and musical training. *J Cogn Neurosci*, **20**, 226-239.

Chen, J.L., Penhune, V.B. & Zatorre, R.J. (2009) The role of auditory and premotor cortex in sensorimotor transformations. *Ann N Y Acad Sci*, **1169**, 15-34.

Chen, J.L., Zatorre, R.J. & Penhune, V.B. (2006) Interactions between auditory and dorsal premotor cortex during synchronization to musical rhythms. *Neuroimage*, **32**, 1771-1781.

Chew, T., Ho, K.A. & Loo, C.K. (2015) Inter- and Intra-individual Variability in Response to Transcranial Direct Current Stimulation (tDCS) at Varying Current Intensities. *Brain Stimul*, **8**, 1130-1137.

Del Olmo, M.F., Cheeran, B., Koch, G. & Rothwell, J.C. (2007) Role of the cerebellum in externally paced rhythmic finger movements. *J Neurophysiol*, **98**, 145-152.

Doumas, M., Praamstra, P. & Wing, A.M. (2005) Low frequency rTMS effects on sensorimotor synchronization. *Exp Brain Res*, **167**, 238-245.

Essens, P. (1995) Structuring temporal sequences: comparison of models and factors of complexity. *Percept Psychophys*, **57**, 519-532.

Essens, P.J. & Povel, D.J. (1985) Metrical and nonmetrical representations of temporal patterns. *Percept Psychophys*, **37**, 1-7.

Filmer, H.L., Ballard, T., Ehrhardt, S.E., Bollmann, S., Shaw, T.B., Mattingley, J.B. & Dux, P.E. (2020) Dissociable effects of tDCS polarity on latent decision processes are associated with individual differences in neurochemical concentrations and cortical morphology. *Neuropsychologia*, **141**, 107433.

Foerster, A., Rocha, S., Wiesiolek, C., Chagas, A.P., Machado, G., Silva, E., Fregni, F. & Monte-Silva, K. (2013) Site-specific effects of mental practice combined with transcranial direct current stimulation on motor learning. *Eur J Neurosci*, **37**, 786-794.

Galea, J.M., Jayaram, G., Ajagbe, L. & Celnik, P. (2009) Modulation of cerebellar excitability by polarity-specific noninvasive direct current stimulation. *J Neurosci*, **29**, 9115-9122.

Geiser, E., Notter, M. & Gabrieli, J.D.E. (2012) A Corticostriatal Neural System Enhances Auditory Perception through Temporal Context Processing. *Journal of Neuroscience*, **32**, 6177-6182.

Gelman, A. & Tuerlinckx, F.A. (2000) Type S error rates for classical and Bayesian single and multiple comparison procedures. *Computational Statistics*, **15**, 373-390.

Giovannelli, F., Innocenti, I., Rossi, S., Borgheresi, A., Ragazzoni, A., Zaccara, G., Viggiano, M.P. & Cincotta, M. (2014) Role of the dorsal premotor cortex in rhythmic auditory-motor entrainment: a perturbational approach by rTMS. *Cereb Cortex*, **24**, 1009-1016.

Grahn, J.A. (2012) See what I hear? Beat perception in auditory and visual rhythms. *Exp Brain Res*, **220**, 51-61.

Grahn, J.A. & Brett, M. (2007) Rhythm and beat perception in motor areas of the brain. *J Cogn Neurosci*, **19**, 893-906.

Grahn, J.A. & Brett, M. (2009) Impairment of beat-based rhythm discrimination in Parkinson's disease. *Cortex*, **45**, 54-61.

Grahn, J.A. & McAuley, J.D. (2009) Neural bases of individual differences in beat perception. *Neuroimage*, **47**, 1894-1903.

Grahn, J.A. & Rowe, J.B. (2009) Feeling the beat: premotor and striatal interactions in musicians and nonmusicians during beat perception. *J Neurosci*, **29**, 7540-7548.

Grahn, J.A. & Rowe, J.B. (2013) Finding and Feeling the Musical Beat: Striatal Dissociations between Detection and Prediction of Regularity. *Cerebral Cortex*, **23**, 913-921.

Grahn, J.A. & Schuit, D. (2012) Individual differences in rhythmic ability: Behavioral and neuroimaging investigations. *Psychomusicology: Music, Mind, and Brain*, **22**, 105-121.

Grube, M., Cooper, F.E., Chinnery, P.F. & Griffiths, T.D. (2010a) Dissociation of duration-based and beat-based auditory timing in cerebellar degeneration. *Proc Natl Acad Sci U S A*, **107**, 11597-11601.

Grube, M., Lee, K.H., Griffiths, T.D., Barker, A.T. & Woodruff, P.W. (2010b) Transcranial magnetic theta-burst stimulation of the human cerebellum distinguishes absolute, duration-based from relative, beat-based perception of subsecond time intervals. *Front Psychol*, **1**, 171.

Halsband, U., Ito, N., Tanji, J. & Freund, H.J. (1993) The role of premotor cortex and the supplementary motor area in the temporal control of movement in man. *Brain*, **116 (Pt 1)**, 243-266.

Kornysheva, K. & Schubotz, R.I. (2011a) Impairment of auditory-motor timing and compensatory reorganization after ventral premotor cortex stimulation. *PLoS One*, **6**, e21421.

Kornysheva, K. & Schubotz, R.I. (2011b) Impairment of Auditory-Motor Timing and Compensatory Reorganization after Ventral Premotor Cortex Stimulation. *PLoS ONE*, **6**.

Lafon, B., Rahman, A., Bikson, M. & Parra, L.C. (2017) Direct Current Stimulation Alters Neuronal Input/Output Function. *Brain Stimulation*, **10**, 36-45.

Lewis, P.A., Wing, A.M., Pope, P.A., Praamstra, P. & Miall, R.C. (2004) Brain activity correlates differentially with increasing temporal complexity of rhythms during initialisation, synchronisation, and continuation phases of paced finger tapping. *Neuropsychologia*, **42**, 1301-1312.

Li, Q., Liu, G., Wei, D., Liu, Y., Yuan, G. & Wang, G. (2019) Distinct neuronal entrainment to beat and meter: Revealed by simultaneous EEG-fMRI. *Neuroimage*, **194**, 128-135.

López-Alonso, V., Fernández-del-Olmo, M., Costantini, A., Gonzalez-Henriquez, J.J. & Cheeran, B. (2015) Intra-individual variability in the response to anodal transcranial direct current stimulation. *Clinical Neurophysiology*, **126**, 2342-2347.

Macar, F., Anton, J.-L., Bonnet, M. & Vidal, F. (2004) Timing functions of the supplementary motor area: an event-related fMRI study. *Cognitive Brain Research*, **21**, 206-215.

Malcolm, M.P., Lavine, A., Kenyon, G., Massie, C. & Thaut, M. (2008) Repetitive transcranial magnetic stimulation interrupts phase synchronization during rhythmic motor entrainment. *Neurosci Lett*, **435**, 240-245.

McAuley, J.D., Henry, M.J. & Tkach, J. (2012) Tempo mediates the involvement of motor areas in beat perception. *Ann N Y Acad Sci*, **1252**, 77-84.

Nitsche, M.A. & Paulus, W. (2000) Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol*, **527 Pt 3**, 633-639.

Nitsche, M.A., Schauenburg, A., Lang, N., Liebetanz, D., Exner, C., Paulus, W. & Tergau, F. (2003) Facilitation of implicit motor learning by weak transcranial direct current stimulation of the primary motor cortex in the human. *J Cogn Neurosci*, **15**, 619-626.

O'connell, N.E., Cossar, J., Marston, L., Wand, B.M., Bunce, D., Moseley, G.L. & De Souza, L.H. (2012) Rethinking clinical trials of transcranial direct current stimulation: participant and assessor blinding is inadequate at intensities of 2mA.

Patel, A.D., Iversen, J.R., Chen, Y. & Repp, B.H. (2005) The influence of metricality and modality on synchronization with a beat. *Exp Brain Res*, **163**, 226-238.

Picard, N. & Strick, P.L. (2001) Imaging the premotor areas. *Curr Opin Neurobiol*, **11**, 663-672.

Pollok, B., Rothkegel, H., Schnitzler, A., Paulus, W. & Lang, N. (2008) The effect of rTMS over left and right dorsolateral premotor cortex on movement timing of either hand. *European Journal of Neuroscience*, **27**, 757-764.

Povel, D.J. & Okkerman, H. (1981) Accents in equitone sequences. *Percept Psychophys*, **30**, 565-572.

Purpura, D.P. & McMurtry, J.G. (1965) Intracellular Activities and Evoked Potential Changes during Polarization of Motor Cortex. *J Neurophysiol*, **28**, 166-185.

Rao, S.M., Harrington, D.L., Haaland, K.Y., Bobholz, J.A., Cox, R.W. & Binder, J.R. (1997) Distributed neural systems underlying the timing of movements. *J Neurosci*, **17**, 5528-5535.

Ridding, M. & Ziemann, U. (2010) Determinants of the induction of cortical plasticity by non-invasive brain stimulation in healthy subjects. *The Journal of physiology*, **588**, 2291-2304.

Ross, J., Iversen, J. & Balasubramaniam, R. (2018a) Dorsal Premotor Contributions to Auditory Rhythm Perception: Causal Transcranial Magnetic Stimulation Studies of Interval, Tempo, and Phase. *bioRxiv*, 368597.

Ross, J.M., Iversen, J.R. & Balasubramaniam, R. (2018b) The Role of Posterior Parietal Cortex in Beat-based Timing Perception: A Continuous Theta Burst Stimulation Study. *J Cogn Neurosci*, **30**, 634-643.

Ruspantini, I., Maki, H., Korhonen, R., D'Ausilio, A. & Ilmoniemi, R.J. (2011) The functional role of the ventral premotor cortex in a visually paced finger tapping task: a TMS study. *Behav Brain Res*, **220**, 325-330.

Schubotz, R.I. & von Cramon, D.Y. (2001) Interval and ordinal properties of sequences are associated with distinct premotor areas. *Cereb Cortex*, **11**, 210-222.

Sowinski, J. & Dalla Bella, S. (2013) Poor synchronization to the beat may result from deficient auditory-motor mapping. *Neuropsychologia*, **51**, 1952-1963.

Teki, S., Grube, M. & Griffiths, T.D. (2011a) A unified model of time perception accounts for duration-based and beat-based timing mechanisms. *Front Integr Neurosci*, **5**, 90.

Teki, S., Grube, M., Kumar, S. & Griffiths, T.D. (2011b) Distinct neural substrates of duration-based and beat-based auditory timing. *J Neurosci*, **31**, 3805-3812.

Turi, Z., Csifcsák, G., Boayue, N.M., Aslaksen, P., Antal, A., Paulus, W., Groot, J., Hawkins, G.E., Forstmann, B. & Opitz, A. (2019) Blinding is compromised for transcranial direct current stimulation at 1 mA for 20 min in young healthy adults. *European Journal of Neuroscience*, **50**, 3261-3268.

Ullen, F., Forssberg, H. & Ehrsson, H.H. (2003) Neural networks for the coordination of the hands in time. *J Neurophysiol*, **89**, 1126-1135.

Vollmann, H., Conde, V., Sewerin, S., Taubert, M., Sehm, B., Witte, O.W., Villringer, A. & Ragert, P. (2013) Anodal transcranial direct current stimulation (tDCS) over supplementary motor area (SMA) but not pre-SMA promotes short-term visuomotor learning. *Brain Stimulation*, **6**, 101-107.

Wetzels, R., Matzke, D., Lee, M.D., Rouder, J.N., Iverson, G.J. & Wagenmakers, E.J. (2011) Statistical Evidence in Experimental Psychology: An Empirical Comparison Using 855 t Tests. *Perspect Psychol Sci*, **6**, 291-298.

Winkler, I., Háden, G.P., Ladinig, O., Sziller, I. & Honing, H. (2009) Newborn infants detect the beat in music. *Proceedings of the National Academy of Sciences*, **106**, 2468-2471.

Yee, W., Holleran, S. & Jones, M.R. (1994) Sensitivity to event timing in regular and irregular sequences: influences of musical skill. *Percept Psychophys*, **56**, 461-471.