

The Role of Posterior Parietal Cortex in Beat-based Timing Perception: A Continuous Theta Burst Stimulation Study

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Abstract

■ There is growing interest in how the brain's motor systems contribute to the perception of musical rhythms. The Action Simulation for Auditory Prediction hypothesis proposes that the dorsal auditory stream is involved in bidirectional interchange between auditory perception and beat-based prediction in motor planning structures via parietal cortex [Patel, A. D., & Iversen, J. R. The evolutionary neuroscience of musical beat perception: The Action Simulation for Auditory Prediction (ASAP) hypothesis. *Frontiers in Systems Neuroscience*, 8, 57, 2014]. We used a TMS protocol, continuous theta burst stimulation (cTBS), that is known to down-regulate cortical activity for up to 60 min following stimulation to test for causal contributions to beat-based timing perception. cTBS target areas included the left posterior parietal cortex (IPPC), which is part of the dorsal auditory stream, and the left SMA (ISMA). We hypothesized that down-regulating IPPC would interfere

with accurate beat-based perception by disrupting the dorsal auditory stream. We hypothesized that we would induce no interference to absolute timing ability. We predicted that down-regulating ISMA, which is not part of the dorsal auditory stream but has been implicated in internally timed movements, would also interfere with accurate beat-based timing perception. We show ($n = 25$) that cTBS down-regulation of IPPC does interfere with beat-based timing ability, but only the ability to detect shifts in beat phase, not changes in tempo. Down-regulation of ISMA, in contrast, did not interfere with beat-based timing. As expected, absolute interval timing ability was not impacted by the down-regulation of IPPC or ISMA. These results support that the dorsal auditory stream plays an essential role in accurate phase perception in beat-based timing. We find no evidence of an essential role of parietal cortex or SMA in interval timing. ■

INTRODUCTION

When listening to musical rhythms, we actively engage with the auditory streams by making timing predictions about underlying periodicities. It has been argued that we experience rhythmic events in relation to an internal scaffolding of temporal predictions (Iversen & Balasubramaniam, 2016; Repp & Su, 2013; Repp, 2005). Periodic timing predictions are central to beat-based time perception in a manner that is distinct from the mechanisms of absolute interval timing (Iversen & Balasubramaniam, 2016; Ross, Iversen, & Balasubramaniam, 2016; Patel & Iversen, 2014; Teki, Grube, & Griffiths, 2012; Teki, Grube, Kumar, & Griffiths, 2011).

Making beat-based timing predictions relies, of course, on the auditory system but has also been shown to reliably activate motor structures, including premotor cortex (Chen, Penhune, & Zatorre, 2009), even in the absence of overt movement (Teki et al., 2012; Grahn & Brett, 2007). A key outstanding question is, what is the role of motor systems in beat perception (Zatorre, Chen, & Penhune, 2007)? Is activity in motor planning areas of the brain during rhythm perception merely a passive

byproduct of unexecuted motor acts or does it play some more active role in shaping auditory perception? There is mounting evidence for the later possibility that making and maintaining beat-based timing predictions requires interaction between auditory and motor systems (Zatorre et al., 2007; reviewed in Ross et al., 2016).

It has long been suggested that beat-based timing utilizes an internal predictive model, meaning that we make timing predictions that are adjusted based on error between the predictions and the experienced auditory feedback (Iversen & Balasubramaniam, 2016; Repp & Su, 2013; Repp, 2005). The theory that perception of rhythmic timing incorporates prediction and adjustment based on sensory feedback is supported by the following four observations. First, negative mean asynchrony in synchronized finger-tapping tasks can be explained by inaccurate predictions of when the beat should be, and error correction suggests that we adjust for these inaccuracies (Repp, 2005; Woodrow, 1932; Miyake, 1902). Second, rhythm perception is tempo flexible, meaning that we adjust for changes in timing, perhaps based on inaccurate predictions and using error correction mechanisms (Patel & Iversen, 2014; McAuley, Jones, Holub, Johnston, & Miller, 2006; London, 2004; van Noorden & Moelants, 1999; Hanson, Case, Buck, & Buck, 1971). Further evidence for top-down influence, such as described by

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internal predictive models, on rhythm perception has been demonstrated by showing perceptual susceptibility to willful control (Iversen, Repp, & Patel, 2009) and improved perceptual acuity of events that occur on the beat (Su & Pöppel, 2012). See Ross et al. (2016) for a more detailed review of these four pieces of evidence supporting that rhythm perception involves prediction and correction. This process of prediction and error correction is similar to the process described for internal predictive models for body movement planning and execution.

The notion of a predictive model does not necessarily imply motor system involvement, but there is growing evidence that timing predictions are made using the motor system (Morillon & Baillet, 2017; Arnal, 2012; Teki et al., 2011, 2012) and are adjusted continuously based on the perceived auditory stream information (Repp, 2005). These predictive models also critically influence ongoing auditory perceptual processing, conceptually requiring bidirectionality in auditory–motor interactions (Manning & Schutz, 2013; Iversen et al., 2009; Phillips-Silver & Trainor, 2005, 2007). Bidirectional interchange between auditory and motor processes is supported by neuroanatomical and behavioral evidence (Blecher, Tal, & Ben-Shachar, 2016; Kotz, Brown, & Schwartz, 2016; Grahn & Brett, 2007), beta band modulation in EEG studies of rhythm perception (Fujioka, Trainor, Large, & Ross, 2012; Iversen et al., 2009), and perceptual data of patients with motor and premotor lesions (Grube, Cooper, Chinnery, & Griffiths, 2010; Grahn & Brett, 2009).

Cerebellum, premotor areas, SMA, and the BG have frequently been implicated in imaging studies of beat-based perception and synchronization (Grahn & Brett, 2007, 2009; Zatorre et al., 2007). Zatorre, Chen, and Penhune (2007) suggested that higher-level timing control involves BG, dorsal premotor cortex, and SMA and that the cerebellum is involved in more fine-grained timing correction. It is thought that functionally segregated timing networks exist for absolute timing of intervals and beat-based timing (Grube, Cooper, et al., 2010; Grube, Lee, Griffiths, Barker, & Woodruff, 2010), which involves prediction (Iversen & Balasubramaniam, 2016; Patel & Iversen, 2014), but these timing networks have not been mapped. Grube, Cooper, et al. (2010) showed detriments in interval timing perception with chronic cerebellar dysfunction, but no effect on beat-based timing. Grube, Lee, et al. (2010) used a causal design with TMS to show that down-regulation of medial cerebellum results in detriments in interval timing perception, but not in their test of beat-based timing. These studies suggest that cerebellum is actively involved in absolute timing and that there might be functionally distinct networks for interval timing and beat-based timing (Teki et al., 2011, 2012; Grube, Cooper, et al., 2010; Grube, Lee, et al., 2010).

The BG, premotor areas, and SMA are connected via a BG–thalamo–premotor loop (Alexander, Crutcher, & DeLong, 1990; Schell & Strick, 1984). Patients with Parkinson disease, which is characterized by cell death

of dopamine-producing cells in the substantia nigra of the BG, exhibit underactivity in structures that receive BG output, such as SMA and pre-SMA (Haslinger et al., 2001; Jahanshahi et al., 1995; Rascol et al., 1994). Dopamine therapies have been shown to modulate activity in some patients in BG, SMA, and pre-SMA (Haslinger et al., 2001; Rascol et al., 1994). Grahn and Brett (2009) showed that patients with Parkinson disease can exhibit impairments in beat-based timing discrimination, but it is unclear whether this impairment is due to lesions in BG or underactivity in SMA or pre-SMA (Grahn & Brett, 2009). It is also unknown how the BG, SMA, and pre-SMA are involved in beat-based timing, but Grahn and Brett (2009) suggest they may be involved in detecting the underlying beat.

The dorsal auditory pathway, connecting auditory and mid to dorsal premotor cortices via parietal regions, has been proposed as a substrate for motor–auditory interactions critical for beat-based time perception in the Action Simulation for Auditory Prediction (ASAP) hypothesis (Patel & Iversen, 2014). ASAP makes two specific claims: that the motor planning system is “necessary” for beat-based perception and that auditory and motor planning cortices interact using bidirectional projections through parietal cortex. Parietal cortex is thus predicted by ASAP to be a critical link in beat-based timing. Although parietal cortex has been less often associated with timing than motor and premotor cortices, it has been implicated in some studies (Pollok, Stephan, Keitel, Krause, & Schaal, 2017; Coull, Cotti, & Vidal, 2016; Coull & Nobre, 2008; Pollok, Gross, Müller, Aschersleben, & Schnitzler, 2005) as well as playing a role in music cognition (Foster, Halpern, & Zatorre, 2013; Zatorre, Halpern, & Bouffard, 2010).

One region that is not explicitly included in the dorsal auditory pathway proposed by the ASAP hypothesis is the SMA. This is surprising because SMA is commonly and consistently implicated in studies of beat-based timing, typically associated with internally guided movements (Chauvigné, Gitau, & Brown, 2014; Chen et al., 2009; Grahn & Brett, 2007, 2009), including continuation timing (Rao et al., 1997). Given this role in internally generated periodicity, it is reasonable to expect that SMA would also play a role in beat perception (Teki et al., 2012).

In the current study, we focus on these two regions, posterior parietal cortex (PPC) and SMA, one predicted to be involved in beat-based time perception by the ASAP hypothesis and the other one not, with the aim of resolving the relationship of these regions to beat perception, and possibly refining the ASAP hypothesis. Although most previous studies have used functional activity measures to point to regions involved in beat perception, such studies cannot directly probe the causal role of such regions. Ultimately, causal manipulation is the only way of directly proving that auditory–motor interactions are bidirectional and the only way of directly testing the

central claim of ASAP that motor regions are causally involved in beat perception. There has been a scarcity of such causal studies attempting to map out a beat-based timing network, which the current study aims to remedy.

Using a causal design complementary to that used by Grube, Lee, et al. (2010), we tested the active role of SMA and PPC in beat-based timing perception. We used a continuous transcranial magnetic theta burst stimulation (cTBS; Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005) applied over the left PPC (lPPC), the left SMA (lSMA), and a sham stimulation condition. Although both right and left hemispheres may be involved in beat-based timing, we focused on the left hemisphere in this study for a number of reasons. Pollok and colleagues have shown a strong left hemisphere role for motor timing (Pollok, Rothkegel, Schnitzler, Paulus, & Lang, 2008). There is some evidence for predictive movement control being lateralized to the dominant hemisphere and muscle stiffness regulation or exploratory motor behavior being lateralized more to the nondominant hemisphere (Kaulmann, Hermsdörfer, & Johannsen, 2017; Yadav & Sainburg, 2014). Our participants were all right-hand dominant, so we decided to focus on left hemisphere targets, although we are planning studies to compare hemispheric differences in beat perception. We measured interval and beat-based timing before and after stimulation. We predicted, based on the arguments presented above, that beat-based timing perception thresholds would increase, indicating decreases in perceptual acuity, with cTBS-induced cortical down-regulation in both lPPC and lSMA. We expected no change in interval timing perception thresholds in any of the conditions, supporting the possibility of functionally distinct timing networks for interval and beat-based timing.

METHODS

Participants

Participants were 25 healthy adults (12 men, 13 women), ages 18–23 years (mean age = 19.8 years, $SD = 1.62$ years), recruited from the University of California, Merced, student population and the Merced, California, local population. All participants were dominantly right-handed and screened for atypical hearing, amusia, and contraindications for TMS including increased risk for seizure, unstable medical problems, metal in the body other than dental fillings, neurological or psychiatric illness, history of syncope, and head or spinal cord surgery or abnormalities (Huang et al., 2005). Participants were asked to remove all metal jewelry before TMS. Fourteen participants reported no musical training or experience. Seven participants reported 5 years or more of musical training or experience (15 years of violin/10 years of guitar, 10 years of piano and guitar, 9 years [4 of guitar and 5 of vocal training], 9 years of piano and clarinet, 7 years [5 of piano and 2 of violin], 6 years [3 of guitar, 1 of piano, and 2 of choir], and 5 years [2 in choir and 3 in band]). The other four participants reported

2 years of violin, less than 1 year of trumpet, 1 year of guitar, and 1 year of piano. Music listening preferences included a wide range of genres spanning pop, hip-hop, rap, alternative/rock, country, classical, R&B, punk, metal, j-pop, jazz, electronic, reggae, and blues. The experimental protocol was carried out in accordance with the Declaration of Helsinki, reviewed by the University of California, Merced, institutional review board, and all participants gave informed consent before testing.

Procedures

Psychoacoustic Testing

When testing for deficits in beat-based perception, it is critical to test if these are merely a consequence of lower-level absolute timing deficits or are truly deficits in relative, beat-based timing. Consequently, in addition to beat timing tests (described below), an adaptive test of absolute interval timing was used to determine a psychoacoustic threshold for detecting differences in timing between two auditory stimuli. This was a single-interval duration discrimination test (Figure 1A), similar to that used by Grube, Lee, et al. (2010) and implemented in The MathWorks' MATLAB (Natick, MA) using custom-designed functions and the Psychophysics Toolbox, Version 3. This perceptual threshold from the interval timing task was used to represent perceptual acuity for interval discrimination. An increase in threshold can be interpreted as a decrease in perceptual acuity. Specifically, this threshold indicates the minimum interval duration difference that cannot be correctly identified as different. Interfering with normal activity in timing networks involved in this timing task would be expected to raise the perceptual threshold determined by this test. Stimulus beeps were created using MATLAB and were 200 Hz pure tones that lasted 0.1 sec each. This test was selected because it is a test of duration-based timing. Each participant performed the test before and immediately after application of cTBS to the selected cortical site.

In this single-interval duration discrimination test, participants were instructed to make a “same” or “different” judgment between a reference interval of variable duration, presented first, and a target interval, presented second, for 50 trials. Intervals refer to the duration of silence between pairs of tones; reference intervals were 300, 360, 420, 480, 560, and 600 msec presented in a randomized order. The initial target interval duration was 90% of the reference interval, and it was adaptively decreased by 6% or increased by 12% after every two consecutive correct or one incorrect response, respectively. Discrimination thresholds were calculated as the mean of the absolute value of the difference between the target and reference interval of the last six incorrect trials, which roughly estimates a correct point of the psychometrical function. The adaptive method we used was a combined transformed and weighted method. It used the one-up

two-down method (Levitt, 1971) with asymmetric step sizes (Kaernbach, 1991) $S_{up} = 2S_{down}$. We propose the equilibrium point is described by $S_{down}P(\text{DOWN}) = S_{up}[1 - P(\text{DOWN})]$, where $P(\text{DOWN}) = [P(X_p)]^2$ as in Levitt (1971). Solving for the convergence point $P(X_p)$ gives $\sqrt{2/3} = 0.816$, meaning this procedure estimates the interval length for which a correct discrimination would be given 81.6% of the time.

Beat Alignment Test, Adaptive Version

Two tests of relative, beat-based timing using musical stimuli were used that adapted in difficulty based on participant performance and determined beat-based timing thresholds for interbeat interval (IBI) changes and phase shifts. These tests were based on the adaptive procedure used by Grube, Lee, et al. (2010) but instead tested musical timing error detection instead of timing discrimination with noncomplex sounds. Beat-based timing thresholds from these timing tasks were used to represent perceptual acuity for changes in IBIs and phase shifts with musical stimuli. An increase in threshold can be interpreted as a decrease in perceptual acuity for detecting these timing changes. Specifically, these thresholds indicate the minimum timing difference that could not be correctly identified as different. See Grube, Lee, et al. (2010) for more details about the adaptive procedure. Interfering with normal activity in timing networks involved in these timing tasks would be expected to raise perceptual thresholds determined by these tests. These tests were implemented in MATLAB using custom-designed functions, the Psychophysics Toolbox, Version 3, and stimuli from the Beat Alignment Test (BAT), Version 2 (Iversen & Patel, 2008). Each participant performed the tests before and after application of cTBS to the selected cortical site.

The BAT (Iversen & Patel, 2008) was designed to test beat perception in a purely perceptual manner that does not require rhythmic movement usually used to assess beat perception. Musical excerpts are presented with an added metronome beep that is either on-beat, with beeps corresponding to the beat, or perturbed in one of two ways, with a tempo manipulation (IBI condition) or an asynchrony, or phase, manipulation (PHA condition). Twelve musical excerpts were taken from several genres (jazz, rock, orchestral). Each is 11 sec in length, 44.1 kHz (mono), and the amplitude ramps up over 500 msec. The musical excerpts were normalized to control for mean, minimum, and maximum amplitude. The beeps were 1 kHz pure tones, 100 msec in length, and start 5 sec after the music starts. The timing of the on-beat beeps were based on taps made by one author (J. R. I.), averaged across six trials to get mean intertap intervals for each interval in each excerpt (BAT Version 2; Iversen & Patel, 2008). Participants were instructed to discriminate between correct and altered IBIs (Phases) in 26 trials each in the IBI (Phase) subtest by responding

after hearing the musical excerpt by button press in a forced-choice task (response alternatives: on-beat or off-beat). Trials 1 and 2 were always on-beat. Trial 3 had an IBI (Phase) that was altered by 10% (30%). For each trial after Trial 3, an incorrect response resulted in moving back in a progression of difficulty and two correct responses in a row resulted in moving forward in a progression of difficulty. A correct response followed by an incorrect response resulted in the next trial using the same level of difficulty (Figure 1B).

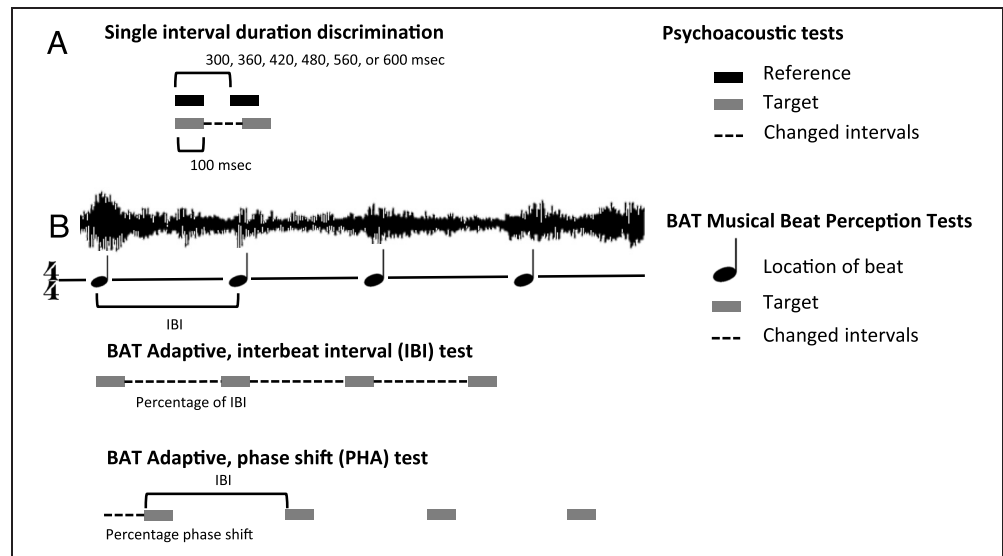
BAT, Adaptive Version (A-BAT) IBI: In the progression of difficulty, lengthened and shortened IBIs were alternated. The progression of difficulty started at a 10% or -10% IBI, followed by 9% or -9% IBI, 8% or -8% IBI, 7% or -7% IBI, an on-beat trial, and then two each of a mixture of positive and negative 6%, 5%, 4%, 3%, 2%, and 1% IBI, with on-beat trials inserted after the first $\pm 4\%$ trial and after the second $\pm 3\%$ trial. The final trials were always on-beat trials but were not used to calculate the threshold. IBI discrimination thresholds were calculated as in our single-interval duration discrimination test, mirroring the method used by Grube, Lee, et al. (2010) as the mean of the absolute value of the IBI deviation amount of the last six incorrect off-beat trials.

A-BAT PHA: In the A-BAT Phase subtest, the superimposed beeps always had the correct tempo but were shifted slightly earlier or later than the on-beat trials. The structure of the test was identical to the IBI test, but with an initial phase shift of $\pm 30\%$, followed by a 20% or -20% phase shift, 15% or -15% phase shift, 10% or -10% phase shift, 9% or -9% phase shift, an on-beat trial, and then a mixture of both positive and negative 8%, 7%, 6%, 5%, 4%, and 3% phase shifts, with on-beat trials inserted after the $\pm 6\%$ trial and after the $\pm 4\%$ trial, and then both a positive and negative 2% phase shift and both a positive and negative 1% phase shift.

TMS

We used a cTBS paradigm, as described by Huang et al. (2005), to down-regulate cortical activity at target locations. The protocol used was a 40-sec train of three pulses at 50 Hz, repeated at 200-msec intervals, for a total of 600 pulses. This cTBS protocol was applied at 80% of the participant's active motor threshold (AMT). AMT was determined for each participant as the lowest stimulator intensity sufficient to produce a visible twitch with single-pulse TMS to left motor cortex in 5 of 10 trials in the first dorsal interosseous (FDI) muscle of the right hand during isometric contraction. High concordance has been shown between using threshold estimations determined with electromyography and visual twitch (Stokes et al., 2005; Pridmore, Fernandes Filho, Nahas, Liberatos, & George, 1998), and visual twitch is often used to determine AMT (Sandrini, Umiltà, & Rusconi, 2011; Göbel, Calabria, Farnè, & Rossetti, 2006; Göbel, Walsh, & Rushworth,

Figure 1. Adaptive timing tasks used for finding perceptual thresholds. (A) Single-interval duration discrimination test. (B) Tests of relative timing using musical stimuli (A-BAT). This is the adaptive version of the BAT, Version 2 (Iversen & Patel, 2008) and is used to determine perceptual thresholds for detecting changes in IBI (lengthening or shortening) and in shifts in phase (forward or backward).



2001), as we have done. Although visible twitch was used to determine AMT, the best location in left motor cortex for right FDI activation was determined by comparing motor-evoked potentials' size and consistency. Motor-evoked potentials were recorded when at rest, with Ag/AgCl sintered electrodes placed over the belly of the FDI muscle with a ground electrode placed over bone near the right elbow. For single-pulse TMS to primary motor cortex, the figure of eight coil (Magstim, D70² double 70 mm coil, Carmarthenshire, UK) was placed tangential to the head at an angle of ~45° from the anterior–posterior midline.

After AMT was determined, cTBS was applied to IPPC, ISMA, or left M1 with the coil facing away from the participant's head in a sham stimulation condition. Participants received all three stimulation conditions, in a randomized order, with a minimum of 7 days between each condition. Magstim Visor 2 3-D motion capture-guided neuronavigation was used to scale each individual participant's brain model to the Talairach brain using head size and shape and to guide stimulation of IPPC and ISMA. We used 3-D coordinates determined from previous literature for IPPC and ISMA as target stimulation sites. Our IPPC target was at Talairach -40, -50, 51, following the example of Krause et al. (2012). These coordinates are consistent with other studies and produced measurable behavioral effects when stimulated with TMS (Krause et al., 2012). Our ISMA target was at Talairach -6, -12, 54, reported by Chauvigné et al. (2014) and determined using an activation likelihood meta-analysis of 43 imaging studies. See Figure 2 for coil placement.

RESULTS

The effect of cTBS to IPPC, ISMA, and with sham stimulation was measured for interval timing and detection of

deviations in IBI and phase relative to the beat of music. Thresholds were compared before (pre) and after (post) stimulation with paired samples *t* tests, adjusted for multiple comparisons using the Benjamini–Hochberg procedure (Benjamini & Hochberg, 1995) and Wilcoxon signed-rank tests (Figure 3). Pre- and postthresholds were also modeled across condition for each test using linear mixed effects models, with a fixed effect for pre-versus poststimulation and random effects for condition and for participant (which assumes a different baseline or mean threshold for each participant and accounts for intersubject variability). *p* values were obtained by likelihood ratio tests of the full model with the effect in question against the model without the effect in question (Winter, 2013). Change in threshold was calculated as the difference of post- to prestimulation thresholds for

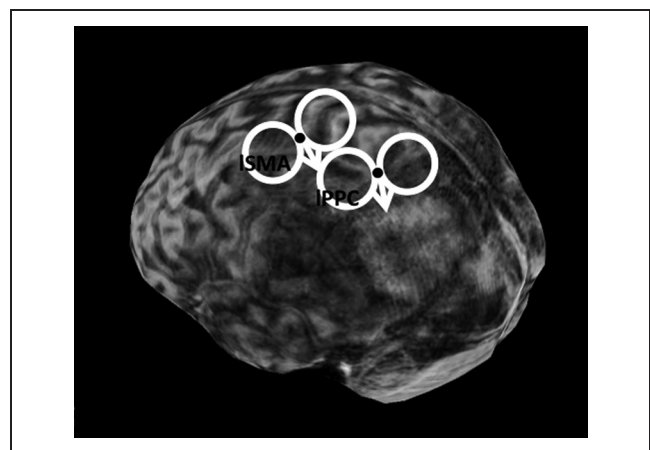


Figure 2. Stimulation sites and coil orientations for ISMA and IPPC conditions. Center of coil was placed at Talairach -6, -12, 54 for ISMA and -40, -50, 51 for IPPC, with the coil facing anteriorly at ~45° from the anterior–posterior midline (Janssen, Oostendorp, & Stegeman, 2015).

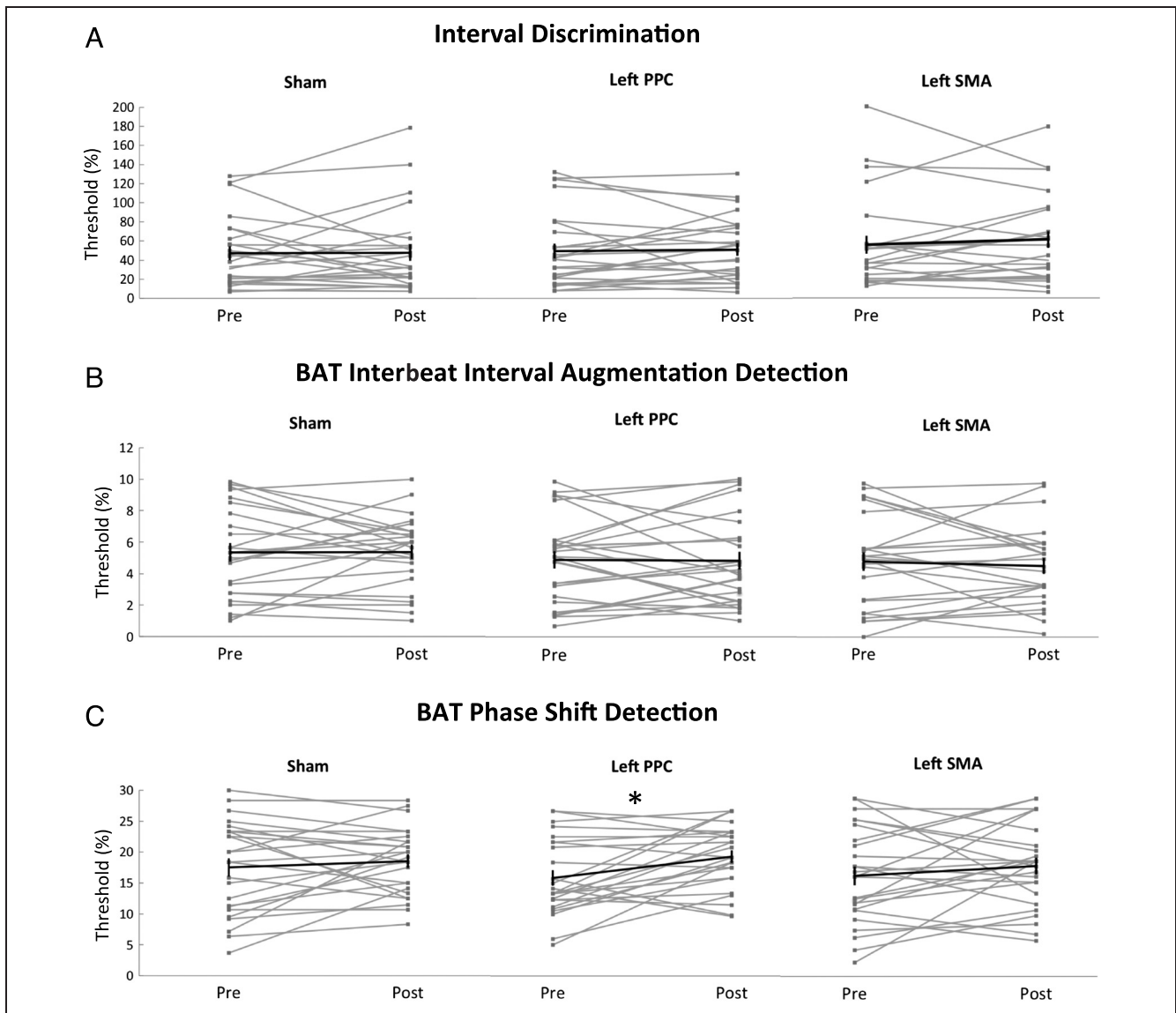


Figure 3. Individual (gray) and mean (black) pre- and post-cTBS thresholds for the three timing tasks in the two stimulation conditions and sham stimulation. Error bars represent ± 1 standard error from the mean. (A) Single-interval duration discrimination. (B) IBI deviation detection with musical stimuli (A-BAT IBI). (C) Phase shift detection with musical stimuli (A-BAT Phase). There was an increase in detection thresholds pre- to poststimulation in phase shift detection with musical stimuli with cTBS to left PPC ($t(24) = -2.998, p = .006$; Cohen's $d_z = .600$, Hedge's $g_{av} = .592$; $Z = -2.501, p = .012$), marked with an asterisk. This effect remained statistically significant after controlling for the three multiple comparisons (Benjamini & Hochberg, 1995).

each test and each condition, with a greater difference indicating worsening of performance after stimulation (Figure 4).

Single-interval Duration Discrimination

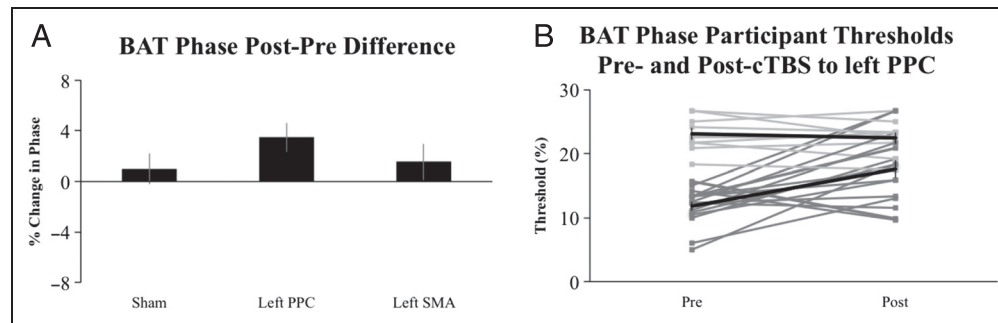
Participant thresholds for pretests ($47.24 \pm 5.42\%$) and posttests ($50.39 \pm 6.17\%$) were within the expected range based on thresholds reported in Grube, Lee, et al. (2010), although our average is somewhat higher than the average reported by Grube, Lee, et al. (2010). See Figure 3A for individual participants' and mean thresholds. As expected, there were no significant changes pre- to poststimulation in single-interval duration discrim-

ination in the sham condition ($t(24) = .418, p = .680$; $Z = -.874, p = .382$) or with cTBS to lSMA ($t(24) = .926, p = .364$; $Z = -.901, p = .367$) or lPPC ($t(24) = .751, p = .451$; $Z = -.659, p = .510$). The linear mixed effects model supports no change from pre- to poststimulation across the three conditions ($\chi^2(1) = .621, p = .431$). These results indicate that cTBS did not cause deficits in single-interval perception.

A-BAT IBI Deviation Detection

Participant thresholds for pretests ($5.00 \pm 0.17\%$) and posttests ($4.89 \pm 0.25\%$) were within the expected range.

Figure 4. (A) Threshold differences pre- to poststimulation for the A-BAT Phase shift detection task in the two stimulation conditions and sham stimulation. Differences are post-pre. Error bars represent ± 1 standard error from the mean. (B) Individual participant thresholds from the A-BAT Phase shift detection subtest showing good performers (dark gray) and poor performers (light gray) and mean thresholds for the two groups (black). Error bars represent ± 1 standard error from the mean.



See Figure 3B for individual participants' and mean thresholds. There were no significant changes pre- to poststimulation in IBI deviation detection with musical stimuli in the sham condition ($t(24) = -.063, p = .951; Z = .000, p = 1.000$) or with cTBS to ISMA ($t(24) = .650, p = .522; Z = -.296, p = .767$) or IPPC ($t(24) = .132, p = .896; Z = -.054, p = .957$). The linear mixed effects model supports no change from pre- to poststimulation across the three conditions ($\chi^2(1) = .139, p = .709$). These results indicate that cTBS did not cause deficits in altered IBI detection with music stimuli.

A-BAT Phase Shift Detection

Participant thresholds for pretests (16.47% shift \pm 0.53%) and posttests (18.47% shift \pm 0.51%) indicate that our participants were generally worse at detecting click-track phase shifts than they were at detecting IBI deviations. See Figure 3C for individual participants' and mean thresholds. There was an increase in phase shift detection thresholds pre- to poststimulation following cTBS to IPPC ($t(24) = -2.998, p = .006$; Cohen's $d_z = .600$, Hedge's $g_{av} = .592; Z = -2.501, p = .012$). Effect size was calculated following Lakens (2013). This effect remained statistically significant after controlling for multiplicity (three multiple comparisons) with a false discovery rate of 0.05, following the Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995). In contrast, there were no changes in phase shift detection following the sham cTBS condition ($t(24) = -.818, p = .421; Z = -.602, p = .547$) or with cTBS to ISMA ($t(24) = -1.063, p = .298; Z = -1.072, p = .284$). The linear mixed effects model supports a significant change from pre- to poststimulation across the three conditions ($\chi^2(1) = 5.837, p = .016$).

The threshold increase after cTBS to IPPC translates to an average of 21.9% increase in phase shift needed to detect that the metronome was off-beat ((post-cTBS - pre-cTBS) / pre-cTBS). Interestingly, there was considerable

intersubject variability in baseline performance on this A-BAT Phase shift test and the appearance of a bimodal distribution, leading to the impression of two groups that were differentially effected by IPPC down-regulation: Only those participants with relatively good baseline performance suffered after cTBS. Figure 3C shows individual participants' thresholds. Sixteen of the 25 participants had pre-cTBS thresholds of below 16%, which we consider as good performance on this task. These participants' performance was most influenced by the application of cTBS to IPPC, bringing their thresholds up into the range of the poor performing participants. For these 16 participants with good baseline sensitivity to phase shift, there was a 49.1% increase in phase shift needed to detect that the metronome was off-beat after cTBS to IPPC. The remaining 9 of 25 participants performed similarly poorly post-cTBS. A regression analysis of baseline performance and performance decrement after cTBS revealed a relationship between increasing threshold and decreasing TMS-induced change in threshold ($r = -0.637, p = .001$). Interestingly, it does not appear that musical training was related to performance in the task because both poor performing and good performing groups had members with musical training and members without musical training. See Figure 4B for good and poor performers' thresholds.

DISCUSSION

Using focal down-regulation of cortex with cTBS, the present experiment tested the roles of ISMA and IPPC in a range of timing tasks: absolute interval timing perception and detection of altered IBIs and phase shifts in musical timing. We found a significant effect of cTBS to IPPC on phase shift detection in the musical timing task (Figure 3C), and no other effects were found. Performance was worse for detecting timing delay/advance (phase shift) relative to the musical beat as indicated by an increased detection threshold. This indicates a

decrease in perceptual acuity in judging stimulus timing relative to a musical beat. These findings demonstrate that IPPC plays a causal role in accurate beat-based timing, directly supporting the ASAP hypothesis' prediction that the auditory dorsal stream (which includes PPC) plays a causal role in auditory beat perception. IPPC is suggested to play an active role in beat-based timing by virtue of its gateway role in the dorsal auditory pathway, with bidirectional projections between auditory and motor planning cortices. Interestingly, IPPC seems to be involved primarily in participants with better pre-cTBS phase shift detection performance, suggesting that it may have a role in making fine distinctions in beat phase.

Given past results showing the involvement of SMA in beat-based perception and synchronization (Chauvigné et al., 2014; Chen et al., 2009; Grahn & Brett, 2007, 2009), it is surprising that our tests of beat-based timing were not negatively affected by cTBS down-regulation of ISMA. These results, considered together, suggest that the BG–thalamo–premotor loop and the dorsal auditory stream may be involved in different aspects of beat-based timing. They suggest that SMA and pre-SMA implications in beat-based timing could represent down-stream effects of activity in the BG and not causal roles of SMA and pre-SMA for this type of timing perception. Coull and Nobre (2008) propose that cortical circuits connecting premotor to parietal regions are recruited for temporal expectation. They also propose that absolute timing relies more heavily on BG circuits, with SMA coactivation being context dependent. However, it is not clear from their work as to which contexts are necessary for coactivation. The present results suggest that SMA might not have a direct and active role in beat perception. The exact role of SMA in these networks needs careful examination through both imaging and causal investigations.

The present findings also support past work arguing for functionally segregated timing networks for absolute and relative timing (Teki et al., 2012; Grube, Lee, et al., 2010). We did not find any effects of cTBS to ISMA or IPPC in a test of absolute timing. This test of absolute timing was modeled after the test used in Grube, Lee, et al. (2010) with which participants showed poorer performance after cTBS to medial cerebellum. Grube, Lee, et al. (2010) demonstrated a specific cerebellar contribution to absolute timing, and we found no evidence for causal contributions of IPPC or ISMA to absolute timing. However, although our test of absolute timing was similar to the test used by Grube, Lee, et al. (2010), the adaptive method was not the same and targeted a slightly different target threshold and, therefore, cannot provide a perfect dissociation.

We demonstrate a specific parietal contribution to relative timing on a musical phase detection test. Although parietal cortex has been implicated in imaging studies of beat perception (Pollok et al., 2005) and the dorsal auditory stream connects auditory and premotor areas by way of parietal cortex and has been proposed to be involved in beat perception (Patel & Iversen, 2014), the mecha-

nisms that involve PPC are undetermined. Zatorre et al. (2007) discussed ventral and dorsal pathways projecting from primary auditory cortex and the possible functional roles of these pathways. One suggestion is that ventral and dorsal auditory projections parallel ventral and dorsal visual streams (Rauschecker & Tian, 2000). In this model, ventral pathways support time-independent object processing, and dorsal pathways support spatial processing and tracking time-varying events (Warren, Wise, & Warren, 2005; Zatorre & Belin, 2005; Belin & Zatorre, 2000), which, as Zatorre et al. (2007) suggest, is most likely to connect with motor areas because body movements exist in time and space.

The suggestion that PPC is involved in predictive mechanisms involving motor networks is not without precedent: PPC has been suggested to play a role in exploratory or anticipatory movements in the control of balance (Kaulmann et al., 2017), along with prefrontal and primary motor cortices (Mihara et al., 2012). Kaulmann et al. (2017) show that cTBS to right PPC reduces variability in postural sway movements and suggest that this could support that parietal cortex is involved in exploratory or anticipatory movements.

Some insight into what this difference is might be found in the work of Zatorre and colleagues. In a series of fMRI studies, PPC is implicated for temporal manipulation of musical sounds (Foster et al., 2013; Zatorre et al., 2010). In these studies, participants were asked to imagine a familiar tune, listen to a sequence of notes, and decide whether the sequence of notes was the familiar tune played in reverse. The task required participants to imagine a manipulated (time-reversed) version of the melody. Unlike other imaging studies of auditory imagery, which implicate secondary auditory cortex, SMA and inferior frontal areas (see Zatorre & Halpern, 2005, for a review), this study required temporal manipulation of auditory imagery. Parietal cortex as well as right auditory ventrolateral and dorsolateral frontal cortices were active during the mental manipulations (Foster et al., 2013; Zatorre et al., 2010). This suggests that parietal cortex is involved in active engagement with or temporal manipulation of music. Left parietal cortex has also been suggested to play a role in temporal attention (Coull & Nobre, 1998), temporal expectation (Coull & Nobre, 2008), and temporal predictability (Coull et al., 2016), as well as auditory motor synchronization (Pollok et al., 2017).

If PPC is required for beat-based timing in general, then it is surprising that our results do not show negative effects of down-regulation of IPPC on detection of changes in IBIs in the A-BAT IBI test. Some aspect of the A-BAT Phase shift detection appears to use IPPC in a way that the A-BAT IBI detection does not. Although accurate beat perception requires both tempo and phase perception, the two may be supported by separate cognitive processes, evidenced by the differences in error correction in the sensorimotor synchronization work of

Bruno Repp and colleagues. Repp (2005) suggests that the two processes rely on distinct cognitive control mechanisms and possibly different brain circuits. Correction can be based on temporal reference points (such as a metronome or a tap) or on temporal intervals, created by the difference between a metronome and a tap. The A-BAT IBI tests for detection of changes in tempo, but changes in tempo also result in misalignments in phase. We suggest that participants might be using temporal references in the A-BAT IBI and asynchronies in the A-BAT Phase. The IBI and Phase subtests of the A-BAT target different aspects of beat-based timing, and so it is not surprising that they are differentially affected by IPPC stimulation. However, the question remains of how specifically IPPC contributes to phase shift detection.

Research using causal designs should be continued with a goal of mapping out causal interactions in absolute and relative timing networks and to specifically test hypotheses, such as ASAP, which propose beat perception networks. Further investigations are needed to understand the involvement of the BG–thalamo–premotor loop and the dorsal auditory stream in absolute and predictive time perception. These results encourage mechanistic proposals of predictive beat perception that involve parietal cortex, and mechanistic proposals should incorporate the underlying electrophysiology of the dorsal stream through left and right PPC.

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