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Transcranial Magnetic Stimulation to assess Motor System Excitability Fluctuations during Auditory Anticipation and Beat Perception

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Abstract

Humans tend to spontaneously move to the regular beat of musical rhythm. Beat perception is the tendency to sense and anticipate the regular time positions (beats) that movements synchronize with. The neural motor system plays an important role in beat perception, but the dynamics of excitability in the motor system associated with beat perception have not been characterized. This project investigated motor system excitability fluctuations using transcranial magnetic stimulation and electromyography during perception of beat-based and non-beat-based rhythms. We applied single-pulse TMS over the left primary motor cortex of healthy participants as they listened to three types of rhythms that varied in the degree to which they induced beat perception. TMS elicited motor evoked potentials (MEPs) from the first dorsal interosseous muscle. MEP amplitude serves as a proxy for real-time motor system excitability. We hypothesized that during beat perception, motor system excitability may fluctuate at the rate of the perceived beat. We found that beat perception was not associated with anticipatory increases in motor system excitability, or with ongoing fluctuations in excitability at multiple rates associated with the beat. These results inform our understanding of the neural mechanisms of beat perception, as well as potential therapeutic uses of music, for example in Parkinson's disease.

Motor System Excitability Fluctuations during Auditory Anticipation and Beat Perception

Music from cultures across the world contain periodic elements of rhythm that give music its unique features, such as the ability to detect and anticipate beat. Beat perception is this seemingly innate ability to detect these regular underlying “pulses” in music, specifically within rhythms that convey a strong sense of beat (Trippett & Sloboda, 2012). Strong elements of rhythms (regular repeated patterns of movements or sound) often allow us to move intrinsically to the beat of music, whether it is through finger tapping or head bouncing, to the vibrant styles of dance and music that we move to that enrich our cultures and identity. Humans tend to physically move with periodic, rhythmic or regular auditory stimuli (Cameron, Stewart, Pearce, Grube, & Muggleton, 2012). Moreover, musical beat perception is ubiquitous across lifespans. However, our understanding of how it works is still limited from a developmental and mechanistic perspective, especially in regards to the rhythmic complexity and structure of music. Our ability to spontaneously move, with a finger tap or head movement when we to detect and anticipate beats suggests that these behavioral responses indicate the involvement of the motor system in the detection and perception of auditory rhythms, and more specifically beat perception. This study aimed to further understand this capacity to move to the beat by looking into the dynamics of motor system excitability in the presence of a beat.

Auditory- Motor Coupling

Research in music is essential to understanding how the brain processes temporal information of rhythmic patterns during auditory anticipation and beat perception. Understanding how rhythmic patterns, or periodic events, are processed help serve as an index of understanding higher cognitive levels of functioning such as language, speech, and motor control. This research further enhances our ability to understand auditory-motor coupling systems in regards to disease like Parkinson's and other movement disorders. The primary motor cortex (M1), including the premotor (PMC), supplementary motor (SMC) cortical areas project into the basal ganglia, and are involved in the activation and processing of auditory rhythms, with activity modulated by the presence of a perceptible beat and by rhythmic complexity (Cameron et al., 2012). Interestingly, activation of the motor system (the premotor and SMA, basal ganglia, and cerebellum) is present even while participants are listening to music and not executing a movement (Grahn & Brett, 2007). Motor areas are activated even during passive listening and active reproduction (such as a finger tapping) of temporal sequences, suggesting that motor areas in response to beat perception do not require motor movements (Schubotz, Friederici, & Yves von Cramon, 2000).

The degree to which rhythms imply a particular beat can also enhance precision of temporal encoding and ratings of perceived rhythmicity (Cameron et al., 2012). Work by Cameron et al. (2012) showed that the basal ganglia and supplementary motor area (SMA) respond to the presence of a regular beat when subjects were asked to reproduce different types of rhythm sequences. Rhythm reproduction accuracy improved with rhythms types that had a strong beat. Furthermore, prior research by Grahn & Brett (2007) showed that the presence of simple integer relationships between intervals in a sequence may be essential for beat perception, in which the sequence can be encoded perceptually in terms of beats, instead of encoding each individual interval length. This has been shown repeatedly in which rhythms associated with an increasingly stronger beat improve reproduction accuracy (Patel, Iversen, Chen, & Repp, 2014).

The neural motor system plays an active role in the anticipation and perception of periodic events and is active when hearing rhythms (Grahn & Brett, 2007). Furthermore, motor system excitability is greater when listening to rhythms with strong beat than rhythms with weak beat with further activation in the SMA and basal ganglia, which are structures not only involved in motor control, but also in the perceptual processing of auditory stimuli (Cameron et al., 2012). fMRI results by Grahn & Brett (2007) showed that rhythms of complex to simple beat perception elicited higher activity in the basal ganglia and SMA, with activation not only in regards to movement in response to music, but as well as the perception of music without movement. This effect was stronger with strong beat and accents versus weak beat-based music. Thus, the basal ganglia and SMA may then mediate beat perception in response to auditory stimuli. This has been further investigated in functional connectivity studies in which connectivity in brain areas involved in the auditory-motor coupling systems increases as the beat strength increases. Grahn & Rowe, (2009) have suggested that the putamen, SMA, and PMC are engaged in a cortico-subcortical network which is responsible for the analysis of temporal sequences, as well as the prediction or internal generation of beats.

Furthermore, fMRI studies have shown increased connectivity between the superior temporal gyrus (an important component of the auditory system) and SMA and PMA when individuals listened to rhythms with a strong beat (Grahn & Rowe, 2009). They also showed that this connectivity was significantly increased in individuals with more than five years of musical training, suggesting this may affect beat perception, which is a measure this study took into consideration. Zatorre, Chen, & Penhune, (2007) have shown that auditory-premotor interactions, in particular, underlie the temporal predictions involved in rhythm perception. Moreover, the PMC evolved for the purpose of timing in sequences, both in motor system planning and auditory predictions of acoustic sequences (Patel & Iversen, 2014). Therefore, simulating periodic movement in motor planning regions provides a signal that helps increase the ability of the auditory-motor coupling system to predict upcoming beats (Large, Herrera, & Velasco, 2015).

Imaging studies have helped understand how the motor system is involved in beat perception, but these techniques are often limited because the spatial resolution vastly undermines the temporal resolution of imaging techniques, even though the auditory system has exceedingly greater temporal resolution than spatial resolution when compared to studies involving the visual system. Electrophysiology work has shown that beat perception modulates endogenous neural activity at the frequency of the beat, in which neural (e.g., beta) oscillations can anticipate regular sounds and synchronize to auditory stimuli, providing further support of neural activity in the motor areas in response to a beat (Cameron et al., 2012; Fujioka et al., 2012) In this regard, further understanding beat perception may arise from studies of neural oscillations and entrainment. Henry et al., (2017) suggest that, similar to Cameron et al., (2012) neural oscillations reflect fluctuations in local neuronal excitability, where the amplitude envelope, in the presence of auditory rhythms , of neural oscillations become synchronized with the auditory rhythm through entrainment, which give rise to beat perception. EEG studies, using steady-state evoked potentials can show this entrainment through electro-cortical activity, where the presence of a beat could induce EP`s that are proportional to the frequency of the presented beat (Nozaradan, Peretz, Missal, & Mouraux, 2011). Nozaradan et al., (2011) had participants listen and imagine rhythms of varying complexity, from a march to a waltz, and showed that frequencies of steady-state EPs matched the frequency's of perceived and imagined beat rhythms, suggesting synchronization of the perceived and imagined beat in relation to the stimulus heard. This further illustrates the importance of neural activity oscillating to temporally internalized beat perception of auditory rhythms.

The previous aforementioned study by Fujioka et al., (2012), did an MEG study using tones that occurred at the beat position (isochronous tones), and were presented at regular and increased speed (tempo) intervals. While listening to passive auditory rhythms, they recorded beta band activity in the auditory system (a frequency band that controls timing of neural firing) which showed that the increase in amplitude was tempo-dependent, indicative of internalized timing being required to predict the next tone onset. This further supports beat perception being reliant on internalized timing processes. This is why moving along to a beat helps plan subsequent motor responses to the beat. This study characterized motor system excitability fluctuations during beat perception.

TMS and Motor System Excitability

Transcranial magnetic stimulation (TMS) is a useful method of understanding causal relationships between underlying cortical areas and their function. This non-invasive method supersedes other tools within neuroscience which rely primarily on indirect measures of brain activity (BOLD signal, EEG). It is performed by the passage of an electrical current through a wire coil, which generates a magnetic field, entering the skull passively and leading to the generation of an electrical field within the brain tissue which disrupts or enhances regions of interest by generating action potentials (Nevler & Ash, 2015). In the early 1980s, electrical stimulation of the human motor cortex using TMS rather than scalp electrodes reduced discomfort, but also induces electrical currents within the cerebral cortex without external stimulation which often has uncomfortable side effects. (Zaghi, Heine, & Fregni, 2009)(Merton & Morton, 1980). Since TMS was first validated in studies of mapping motor cortex functioning, it has helped elucidate auditory-motor coupling system by directly stimulating motor areas of the brain. With electromyography (EMG), we can record motor evoked potentials (MEPs) or muscle twitches from action potentials generated by M1. It is important to note that M1 is not directly involved in beat perception, but serves as a proxy for motor system excitability from subsequent areas like the SMA, PMC, and other areas involved in motor movement. We would expect that fluctuations in MEP amplitude size reflects changes in excitability in the motor system. If there is greater the excitability of M1, due to greater activation in premotor cortex and SMA, the we would expect larger MEPs. All things considered, TMS stimulation of M1 then serves as a plausible measure of motor system excitability as subjects listen to auditory rhythms.

MEP measurement of Beat Perception

A study by Cameron, Stewart, Pearce, and Grube (2012) measured TMS-elicited MEPs in ankle-driving muscles of the lower leg while participants listened to metrically strong or weak tone sequences and music. TMS pulses fired synchronously to the beat of strong tone sequences had greater MEP amplitudes than weak tone sequences. Their results suggest listening to metrical strong tone sequences resulted in greater motor system excitability as measured through TMS elicited MEPs. Wilson & Davey, (2002) further showed that music of varying genres (beat based) compared to white noise also have been shown to elicit MEPs in lower leg muscles as participant listened to rhythms with a strong beat. The experiment was set up so that the MEP amplitude size was reduced when executing a movement in this study, and they showed that MEP size between leg muscles was reduced in 11 of the the 12 who simple listened to beat-based music (Wilson & Davey, 2002). Therefore, motor system excitability not only synchronizes to the perceived beat of auditory rhythms, but also does not required executing movements as participants listen to auditory rhythms.. As previously suggested, musical training experience can affect motor system excitability and a study by Stupacher et al., (2013), showed increased excitability compared to controls when listening to music with a strong beat. Henceforth, this study considered the years of formal musical training to examine similar effects. This study sought to extend previous work on how motor system excitability synchronizes to the perceived beat of auditory by looking at the time course of motor system excitability, which has not been characterized during auditory anticipation and beat perception. Single pulse TMS will be applied to the primary motor cortex to generate motor evoked potentials in the right hand. This will be done while the participants listen to rhythmic tone sequences of varying beat strengths: metric simple (strong), metric complex (weak), and non-metric (no beat). To measure motor system excitability changes during beat perception, testing occurred across the beat period. With EMG electrodes applied to the right hand, single pulse TMS was administered over the left primary motor cortex to which an MEPs were generated and measured in the first dorsal interosseous muscle (FDI). The beat structure and tempo acted as independent variables, while the MEP data in response to the TMS treatment acted as the dependent variable. All conditions were within-subject factors.

This study included two behavioral tasks, which consisted of a rhythm reproduction task and beat tapping task, both of which used a subset of rhythms presented during TMS. For beat tapping tasks, participants were asked to tap along to the beat of the stimulus. For reproduction tasks, participants tapped the rhythm they heard after perceiving it. We hypothesized that if TMS elicited MEPs serve as an index of motor system excitability, then larger MEPs will be reflective of greater motor system excitability. We predicted that MEPs elicited by stimulation of the primary motor cortex would be greater when participants were listening to rhythms with a strong beat versus a weak beat rhythm, and for TMS pulses synchronized with the metrical beat compared with randomly timed pulses. For the behavioral tasks, we predicted that for the rhythm reproduction and beat tapping task, reproduction and beat tapping accuracy would be greater for rhythms with a strong beat versus a weak beat rhythm. We further predicted that for the beat tapping task, beat tapping variability would be reduced for rhythms with a strong beat versus a weak beat.

Method

Participants

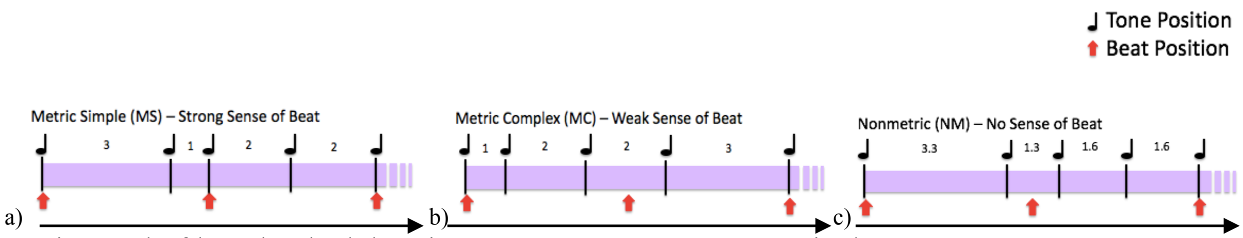
This study included 21participants (9 males, 12 females) between the ages of 19 and 26 years of age (*M* = 21.8, *SD = 1.81)* who were right-handed with normal hearing. Participants were recruited by posters (Appendix A) displayed across Western University campus. Interested participants were provided with a TMS pre-screening form (Appendix B) and were excluded based on criteria that included but were not limited to pacemakers, pregnancy, cerebral aneurysm clips, or a history of neurological disorders (seizures/epilepsy, and/or psychiatric disorders) that require antipsychotics or antidepressant medication which have the potential to induce drowsiness.

Demographics and Questionnaires

Informed consent was given after reading the letter of information (Appendix C), and similar to the pre-screening form, another TMS screening (Appendix D) was given at the beginning of the experiment as well to ensure safety and eligibility in the study. An Edinburgh Handedness Inventory (Oldfield, 1971) questionnaire was also given to assess the level of right-hand dominance. This was only used to assess right hand dominance and was excluded from data analyses. The entire study took an approximate two to three hours and participants were compensated $25/hour for their time.

Auditory Rhythms

Using similar stimuli as described in Cameron et al., (2012) a total of three rhythm types were used. These auditory sequences were composed (using GarageBand) of tones that were 6 ms sound clips of generic snare a drum and consisted of Metric Simple (MS) and Metric Complex (MC) rhythms which were composed of intervals related by integer ratios (1:2:3:4)(Figure 1), and Non-Metric (NM) rhythm which created by reconstructing the rhythm of MS rhythms. Each sequence contained tones consistent in pitch and volume. For the MS rhythms, a tone always occurred on the beat position, eliciting a strong sense of beat. Metric complex tones consisted of tones that matched some beat positions, where the beat position sometimes occurred offset of the tone position, eliciting a weak sense of beat. NM rrhythms were constructed by altering the intervals between tones of the MS rhythm. A third of the intervals (Figure 1c) were increased by half of one unit, creating rhythms that were equal in length and number of tones but simply had irregular timing between tones. The same format had been used by Grahn & Schuit, (2012), which compared MS and MC rhythms to NM rhythms, which showed significantly poorer reproduction and beat perception than the two former conditions. This indicated that NM rhythms conveyed no sense of beat. Overall, there were 14 rhythms for each condition, played at two tempi (700 ms and 900 ms) resulting in a total of 84 randomized rhythms which were 35 – 45 ms in length (depending on the tempo) and heard using fMRI-headphones with eartips to eliminate all possible confounds. Tempo ensures participants paid attention and adjusted their perception of beat accordingly, as research suggests that beat perception within a tempo of 500 to 900 bpm is enough to produce the perception of an underlying beat (Stupacher, Hove, Novembre, Schütz-Bosbach, & Keller, 2013).



1 = interval of length 1 had duration 175 ms or 225 ms, respectively

Figure. 1: Rhythm sequences for Metric Simple (MS), Metric Complex (MC), and Non-Metric (NM) across time.

Materials and Procedure

TMS Stimulation. After eligible participants were given a letter of information and signed consent, participants were seated and were required to passively listen to rhythms of varying beat strength (MS, MC, and NM) while TMS was administered. Single-pulse TMS was administered using a Magstim Rapid magnetic stimulator (Magstim Company Ltd, Camarthenshire, UK) with a figure-eight coil. Because this study was interested in auditory anticipation and beat perception, participants were connected to electromyography (EMG) with electrodes attached to the right hand`s first dorsal interosseous muscles. The primary motor cortex (M1) was approximately located by measuring a participant's head from inion to nasion, and tragus to tragus. The intersection of these lines was then connected and M1 was found by measuring 2 cm anterior and 5 cm to the left from this intersection. The motor threshold (the minimum amount of stimulus intensity required to elicit an MEP 50% of the trials) was obtained by adjusting this threshold for each participant and examining the resulting MEPs that were elicited using EMG (Figure 2). We started initially at 30% and gradually increased by 5% until MT was achieved. Ultimately, MT was set at 110% to ensure proper MEPs were elicited for analysis. In order to assess auditory anticipation and beat perception, the timing of the TMS pulses were fired at asynchronous time points related to the beat position, in which TMS was fired using randomized proportions of .05, .10, .15, and .20 of the inter-beat interval, or onset of the beat. TMS pulses could only be sent a single time every four seconds to prevent over-heating.

Furthermore, TMS pulses were fired only after the first four seconds after the start of an auditory sequence, to ensure the participant was able to perceive an acceptable sense of beat. As the sequences varied by tempo (35 – 45s), TMS pulses were administered six, seven, or eight times per rhythm. For each rhythm type, one TMS pulse occurred once at each of the 100 possible evenly spaced time points within the inter-beat interval. For metric simple and complex rhythms, TMS pulses were elicited always at an interval preceded by a tone in the nearest position to control the local acoustic context. For nonmetric rhythms, TMS pulses were presented in interval proportions preceded by a tone in the nearest "1" position (Figure 1). TMS pulses were separated by 3.5–5 seconds for the 700-ms tempo and 3.9–6.9 seconds for the 900-ms tempo. The greater time between pulses for the slower tempo arises because each rhythm was presented at each of two tempi, and relative spacing of TMS pulses was maintained for the two presentations; thus, absolute spacing of TMS pulses was greater for the slower tempo. Rhythms were presented in a pseudo-random order such that no more than three repetitions of a single rhythm type or tempo condition occurred on sequential trials. MATLAB software was used to elicit TMS triggers (pulses) before the onset of a beat of the associated auditory rhythms (MS, MC, and NM). MEP responses due to TMS stimulations were collected using a Quad AC Amplifier EMG system, which were then sent to the computer using a Micro1401-3 data acquisition unit or CED, where EMG readings (MEPs) were recorded using Signal Software.

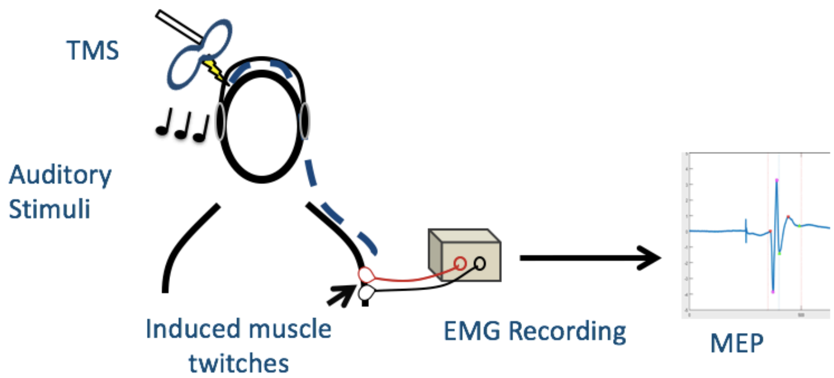


Figure. 2: Experimental set up of protocol used to record behavioural measure of TMS elicited MEPs while participants listened to rhythms of varying complexity (MS, MC, and NM).

Behavioral Tasks

Beat Tapping Task. Participants were asked to complete this task after the TMS stimulation task to assess their ability to perceive a strong and weak sense of beat. Using E-Prime® 2.0 (Psychology Software Tools Inc, Sharpsburg, PA), participants were required to tap along to the beat of rhythms used in the TMS stimulations participants listened to auditory rhythms. Two rhythms from each metric and tempo were randomized for a total of four rhythms of each rhythm type. Participants listened with headphones and were asked to tap along to the beat using the “m” key on the keyboard of the computer. Data was collected on the time between taps and timing of the tapping relative to the start of the sequence. We assessed performance by examining the regularity of a participant's tapping within a trial (co-efficient of variation of inter-tap intervals), and how relative the tapping occurred to the beat positions relative to rhythm tempo (asynchrony to the beat), all of which were calculated using E-Prime® 2.0.

Rhythm Reproduction Task. Participants were required to listen to sampled rhythm clips from the TMS task and asked to tap back the tone onsets. A similar task was used by (Grahn & Brett, 2007) where the ability to reproduce the rhythm was affected by whether or not there was a strong sense of beat, in which metric simple rhythms were easier to reproduce than metric complex and non-metric, respectively. Similar to Grahn & Brett (2007), rhythm tempos were slowed down relative to the TMS task rhythms used while listening. Auditory rhythms in this task included five clips from each beat condition; two at tempi of 920ms and 1080 ms, and one at a tempo of 1000 ms. Slowed tempos ensured that varying difficulties, as a result of rhythm reproduction, came from rhythm perception only. Participants were required to reproduce the rhythm sequences by tapping the “m” key on keyboard of the computer after hearing it twice.

Participants had three attempts to reproduce the rhythm within 20% of the tone onset of the rhythm correctly or else the next randomized sequence was given. This task allowed us to assess the degree of reliability between listening and reproducing the beat, but also to test the prediction that metric simple, or rhythms with a strong sense of beat, were more easily reproduced than more complex ones. Participants were then debriefed and compensated for their time.

Data Analysis

Recorded MEPs were run through MATLAB software to auto-select MEP peaks to create a file containing all the amplitudes of the associated MEPS for each participant. MEPs that did not exceed a 50 μV threshold or were three standard deviations greater from the mean (individually calculated) were deleted. Deleted MEP trials may have resulted from variation in head/coil movement, an average of 30% of the MEPs were deleted across all participants. We characterized fluctuations of standardized and smoothed MEP values (using a sliding window approach) between beat intervals for each participant. We then generated a linear fit model to assess the slopes of the MEP amplitudes to address whether or not excitability increased or decreased before the beat. A two-way 1 (MEP amplitude) x 3 (stimulus condition) repeated measures ANOVA was then conducted to assess slope of linear fit. We then de-trended this data and created cosine fit models, where we generated cosine frequencies related to the stimulus conditions at 1, 2, and 4 times the beat rate for the amplitude of fit (μV) and goodness of fit (R^2). These beat rates related to the integer interval ratios of the generated auditory rhythms, in which a beat rate of 1,2 or 4 times may correspond to the motor system synchronizing to the perceived beat rate of auditory rhythms. For amplitude of fit, we assessed the depths of the MEPs amplitude to address how well the amplitude of MEPs fit the cosine curves. For the goodness of fit, we assessed R^2 values of MEPs to address how the overall data deviated from the cosine curves generated. A two way 3 (Fitted rate) x 3 (Rhythm Type) repeated measures analysis of variance was then conducted to look at the effects of rhythm type and fitted rate for MEP amplitude and R^2 values, respectively. Greenhouse Geisser corrections were applied since repeated measures ANOVAS are susceptible to violating the assumption of sphericity. Behavioral data consisted of a rhythm reproduction task and beat tapping task. The rhythm reproduction tasked was analyzed for mean rhythm reproduction accuracy (number of successful trial passes out of maximum 5 trials) using a one factor repeated measures ANOVA over the three levels of beat strength (MS, MC, and NM) where paired t-test were done wherever there was significance. Likewise, the beat tapping task was analyzed using a one factor repeated measures ANOVA for the two following measures, co-efficient of variation (variation in tapping consistency across trials) and proportion asynchrony (variation in the consistency of tapping in relation to the stimulus condition heard). All statistical tests were set at a p-value of .05. Ten participants where considered musicians as they had more than 2 years of formal music training. Musical experience ranged from 2 – 16 years of experience ($M = 3.65$, SEM = 1.61), and was assessed using a covariate analysis. All statistical analyses were run using IBM SPSS software.

Results

A two-way repeated measures ANOVA for the slope of linear fit found a non-significant interaction for slopes from linear fits to smoothed MEPS, $F(2,30) = 1.58$, $p = .222$. This suggests that slopes did not significantly increase before the beat, although numerically greater for MS ($M = 0.07$, $SEM = .05$) versus MC conditions ($M = 0.02$, $SEM = .04$)(Figure 3). This data was then de-trended and cosine fit models were created using cosine frequencies related to the stimulus conditions at one, two, and four times the beat rate for the amplitude of fit (μV) and goodness of fit (R^2). For amplitude of fit, the results showed a non-significant main effect of rhythm type ($F(2,2) = 1.09$, $p = .345$) and fitted rated ($F(2,2) = .156$, $p = .835$), respectively. A non-significant 3 (fitted rate) x 3 (rhythm type) interaction effect was also found ($F(3,4) = 1.56$, $p = .213$)(Figure 4), suggesting that fluctuations in MEP amplitudes did not differ for rhythm type or fitted rate. When looking at individuals who were deemed musicians (two or more years of formal musical training, we did find a significant interaction, ($F(2,2) = 4.31$, $p = .03$), suggesting that fluctuations in MEP amplitudes significantly differed for rhythm type and fitted rate compared to non-musicians. As for the goodness of fit (R^2), the results also showed a non-significant main effect of rhythm type ($F(2,2) = .993$, $p = .351$) and fitted rated ($F(2,2) = .743$, $p = .484$), respectively. A non-significant 3 (fitted rate) x 3 (rhythm type) interaction effect was also found ($F(3,4) = 1.18$, $p = .327$)(Figure 5), suggesting that fluctuations in MEP amplitudes did not differ selectively for rhythm type or fitted rate.

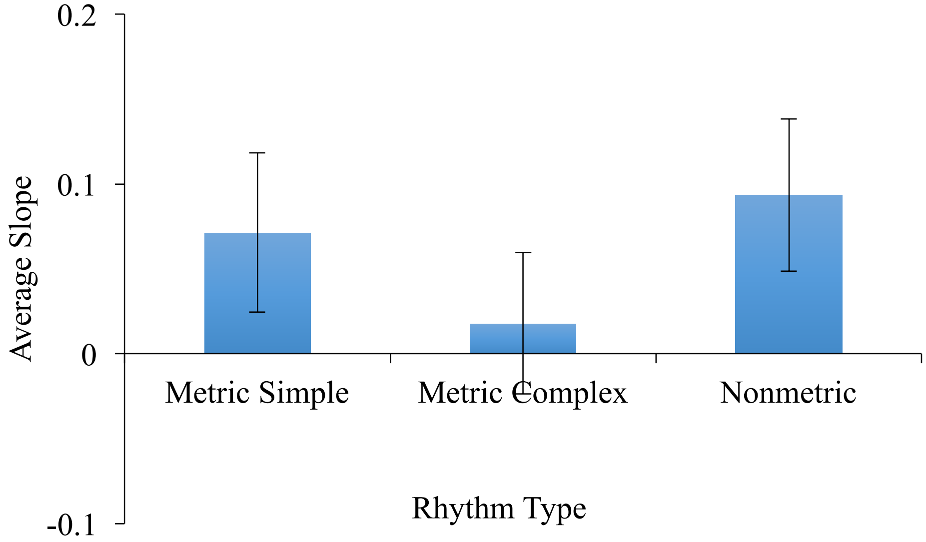


Figure 3. Average slopes from linear fits to smoothed MEPs. Slopes were not significantly different between stimulus conditions (p > .05).

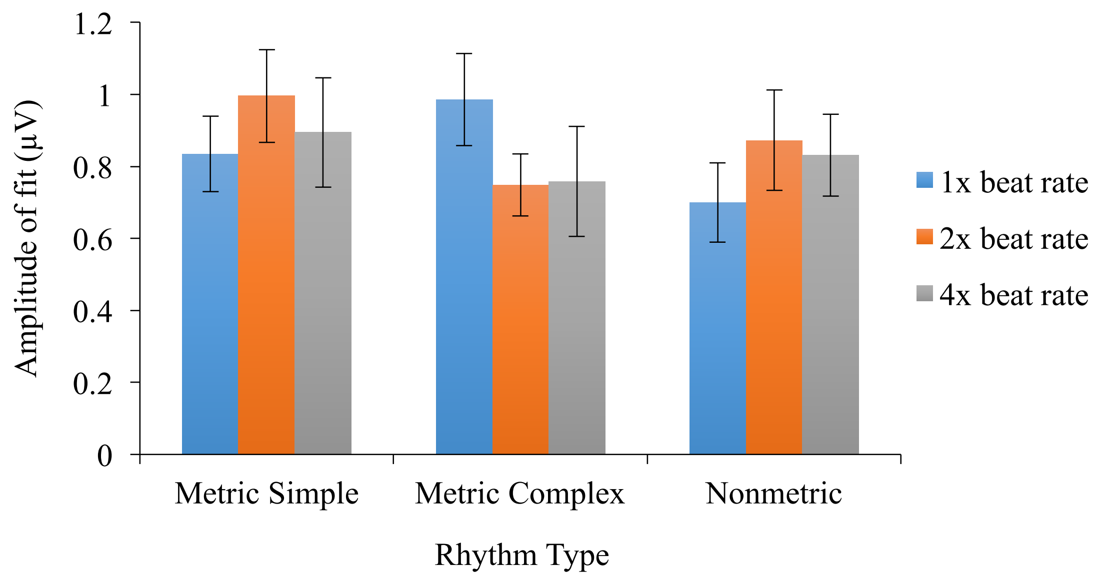


Figure 4. Mean amplitude parameter values (±SEM) from cosine fits to smoothed MEPs as a function of time across the inter-beat interval over two beat cycles showing a non-significant 3 (fitted rate) x 3 (rhythm type) interaction (p > .05)

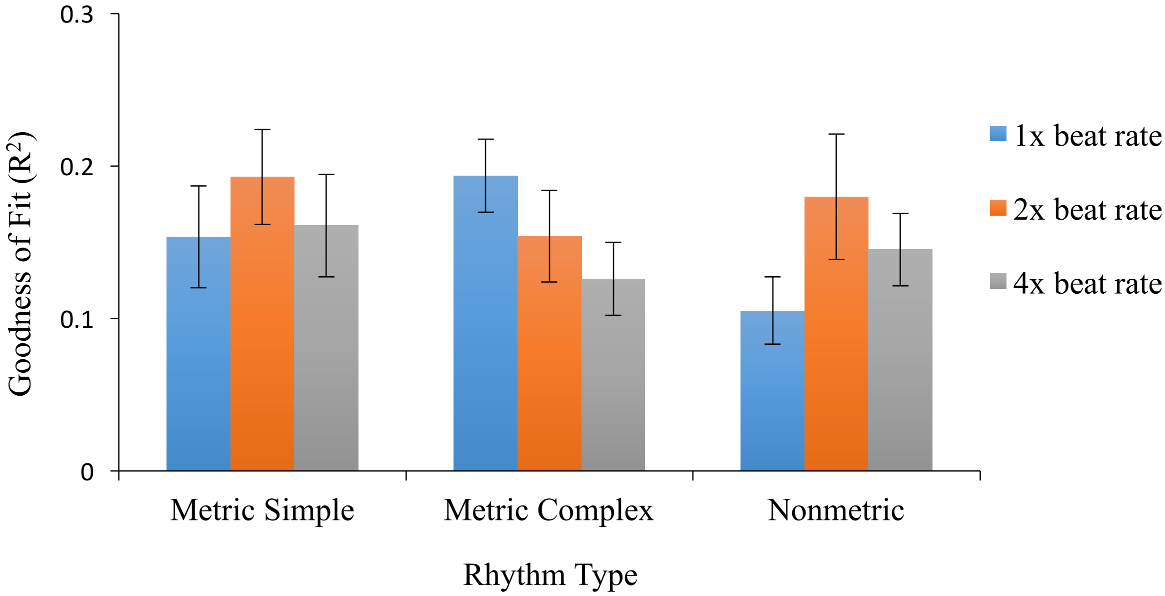


Figure 5. Goodness of fit (R^2) for cosine fits to smoothed MEPs as a function of time across the inter-beat interval over two beat cycles showing a non-significant 3 (Fitted rate) x 3 (Rhythm Type) interaction ($p>.05$).

The behavioral data consisted of a rhythm reproduction task and beat tapping task which were each subjected to a one way repeated measures ANOVA. The results of the rhythm reproduction task showed a significant relationship between rhythm reproduction accuracy and rhythm type, ($F(2,33) = 29.58$, $p < .001$). Furthermore, rhythm reproduction accuracy (number of correct trials out of maximum 5 trials) was significantly greater for MS ($M = 4.42$, $SEM = .254$) vs MC ($M = 3.76$, $SEM = .322$)($t(20) = 2.39$, $p = .03$) and NM ($M = 2.47$, $SEM = .235$) ($t(20) = 9.19$, $p < .001$), respectively. This suggests that rhythms with a strong sense of beat were significantly more accurately reproduced than rhythms with a weak or no sense of beat (Figure 6).

The beat tapping data was analyzed through two observations; co-efficient of variation and proportion asynchrony. The results for the co-efficient of variation (beat tapping consistency across the inter-beat interval) showed a significant relationship between beat tapping variability and rhythm type, ($F(2,2) = 4.11$, $p = .026$)(Figure 7), where where the variability of tapping was significantly lower for the MS condition ($M = .128$, $SEM = .013$) versus MC ($M = .142$, $SEM = .013$) ($t(17) = -2.23$, $p = .01$) and NM ($M = .147$, $SEM = .011$) ($t(17) = -2.47$, $p = .006$), respectively. Furthermore, the proportion asynchrony (beat tapping consistency in relation to the rhythm type heard) also showed a significant interaction between beat tapping accuracy and rhythm type, ($F(2,23) = 12.51$, $p = .001$), where the tapping accuracy is greater (reduced asynchrony) for the MS condition ($M = .206$, $SEM = .008$) versus MC ($M = .246$, $SEM = .004$) ($t(17) = - 3.36$, $p = .001$) and NM ($M = .248$, $SEM = .003$) ($t(17) = -4.34$, $p < .001$)(Figure 8), respectively. This suggests when listening to rhythms with a strong beat (MS), there is reduced tapping variability (more consistent tapping) and greater accuracy.

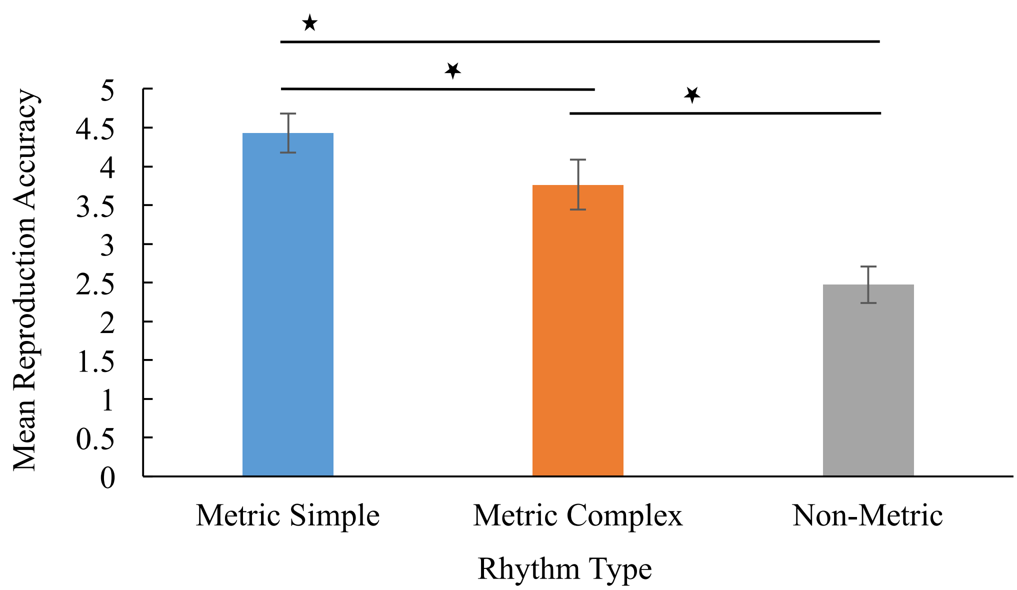


Figure 6. Mean rhythm reproduction accuracy (# of correct trials out of max. 5 trials). Symbols denote significant difference between rhythm types (*p* <.05).

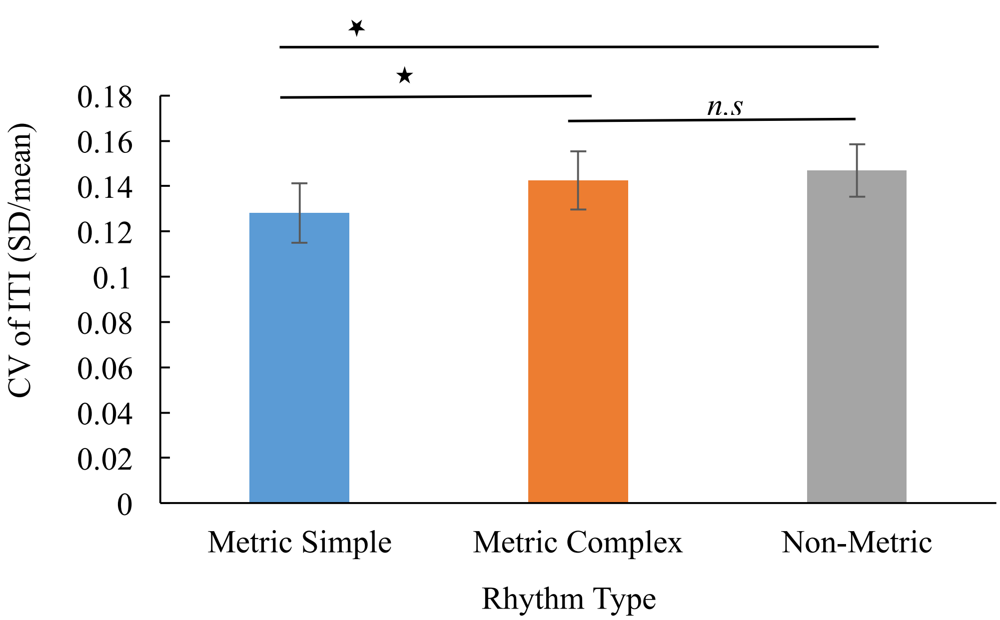


Figure 7. Coefficient of variation (consistency in tapping) across rhythm type of the inter-tap interval. Symbols denote significant differences between rhythm types (*p* <.05).

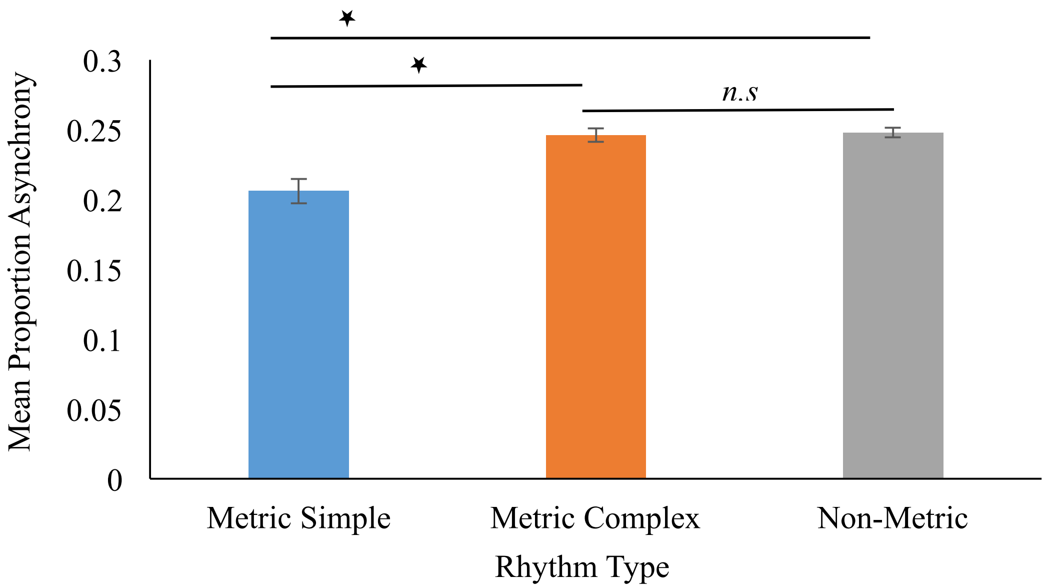


Figure 8. Proportion of asynchrony of the inter-tap interval where the tapping accuracy is greater for MS versus MC rhythm types. Symbols denote significant differences between rhythm types (p <.05).

Discussion

The purpose of this study was to examine how motor system excitability synchronizes to the perceived beat of auditory rhythms by looking at the time course of motor excitability to determine if rhythms of varying beat strength influenced these fluctuations. This was done by using Transcranial Magnetic Stimulation (TMS), which tested for fluctuations in motor system excitability while participants listened to rhythm sequences of varying beat strength. These fluctuations consisted of TMS elicited MEPs across 100 possible time points over the beat interval, which served as a proxy for motor system excitability. The results showed that motor system excitability fluctuations at the beat rate were not significantly greater during listening to metric simple, versus metric complex or non-metric conditions. These results are in contrast to previous work by Grahn & Brett (2007) and Cameron et al., (2012) which used a similar paradigm and found that motor system excitability was greater when listening to rhythms with a strong beat versus a weak beat, suggesting further research is required from this study. As mentioned, M1 does not assess auditory anticipation and beat perception, but modulated excitability from other areas of the motor systems like the supplementary motor area and premotor area.

Because beat perception is hierarchical in nature, it is often referred to as a meter, which means it can be arranged from higher levels of periodicity where the perception can sound like a march, as in the metric simple condition, or more syncopated like in the metric complex condition (Rohrmeier & Koelsch, 2012). However, in this study when participants were asked tap along to the behavioural tasks, beat perception can vary between the metric level a participant synchronizes with in terms of the preferred rate. Likewise, our non-significant results in the MEP fit of fluctuations across rhythm type may include differences in preferred rates. That is to say, individuals listening to a metric simple condition may have different preferred rates of beat perception, such as perceiving the beat in multiples of the fundamental rate (double time or triple time). Motor system excitability may then synchronize to different rates related to rhythm type, so cosine generated curves may not be sensitive to the data analyses. We did see a significant interaction of musical training and motor system excitability fluctuating at the perceived rate of auditory rhythms. Literature has supported that musicians enjoy more syncopated (metric complex) rhythms more than simpler rhythms (Keller & Schubert, 2011). Therefore, beat perception may be more consistent and accurate for having musical experience than not having any. However, future research is required from this study.

Moreover, TMS elicited MEP amplitudes from stimulation of M1, serve as a proxy of motor system excitability from associated areas like the PMC and SMA. Therefore, the lack of results from this study may be due to the variability of measuring M1 as an index of alternate activations of up-stream motor areas. Furthermore, motor system excitability did not significantly increase linearly over the beat interval. The results from this study have also been seen in previous work by Wu et al., (2015), where they did not find a significant main effect or interaction between rhythm type and time before the beat. They examined motor system excitability using similar methods and analyses, which may owe to the variability in TMS-elicited MEP responses, which may have not been sensitive to analyses methods (repeated measures ANOVA) similarly used in this study. Perhaps using more precise methods of localizing M1, better EMG filtering processes, and more sensitive statistical analyses may allow for similar results as previously shown by Grahn & Brett, (2007) and Cameron et al., (2012), where motor system excitability was greater when listening to rhythms with a strong beat.

Furthermore, TMS is highly sensitive and inter-subject variation in skull size and brain anatomy could result in the need to angle and rotate the TMS coil accordingly. In addition, researchers held the coil continuously so movement in the holding positon could have also added to the variability in MEP responses. Another recurring issue in this study was in regards to the MEP data collection process by EMG. Due to set limitation in the EMG filtering process, MEP amplitudes often captured ceiling effects, in which responses exceeded the maximum threshold which ultimately affected the interpretation of MEP amplitudes as a index of motor system excitability. Future studies may want to incorporate better smoothing and filtering processes to more accurately capture MEP responses during auditory anticipation and beat perception. Some research by Schubotz et al., (2000) examined time perception using a go/no-go task. fMRI results showed that compared to baseline, there was greater activity in the PMC, SMA and basal ganglia while listening to auditory rhythms, demonstrating a potential alternative paradigm of examining motor system excitability. The go/no-go task is a measure of response time, where the size of the response in relation to a stimulus heard may reflect motor system excitability.

Although the MEP results do not suggest that there is synchronization of motor system excitability to the beat of musical rhythms, rhythm reproduction and beat tapping data do indicate the involvement of the auditory-motor coupling system. Rhythm reproduction was significantly greater for the metric simple versus metric complex and non-metric, respectively. This suggests that rhythms with a clear beat are more accurately reproduced. Likewise, beat tapping accuracy was greater for metric simple rhythms versus complex and non-metric, with reduced variability than compared to MC and NM conditions. These results seemed likely as the motor system is involved in processing structural and temporal information from environmental stimuli. The metrical structure of rhythms conveys temporal information in the form of weighted peaks of attention that allow the listener to anticipate the next beat and follow rules of expectancy, in which removal of a tone or early onset of a tone creates a change in attention that offers the predictability of a beat (Rohrmeier & Koelsch, 2012). Neuroimaging studies by Maess, Koelsch, Gunter, & Friederici, (2001) showed that musical syntax processing involves the pars opercularis of the inferior frontal gyrus (Brodmann area 44). This area is known to be responsible for the hierarchal processing of syntax of language and action sequences, giving credence to some cognitive operations of processing of musical syntax. Functional connectivity studies have also shown that this area also interacts with the superior part of the pars opercularis, anterior portions of the superior temporal gyrus (major component in auditory processing) and the premotor area. Henceforth, similar to how people process speech syntactically, rhythm reproduction and beat tapping accuracy may reflect similar syntax deciphering processes in terms of the temporal encoding of beat perception as was evident in the behavioural data from this study.

Conclusion

The findings in this study suggest that although behavioral data indicate the involvement of the motor system in rhythm and beat production, we did not observe that motor system excitability fluctuates in correspondence to the perceived beat of auditory rhythms. In relation to previous studies, the mind is very much an anticipator, allowing for the interaction of environmental complexity and incorporating temporal and structural information of rhythms into an internal cognitive schema of musical beat perception.

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APPENDIX A

Western

Western
The Brain and
Mind Institute

Neuroscience of Music Study

The laboratory of Professor Jessica Grahn in the Brain and Mind Institute at the University of Western Ontario is seeking volunteers for a study that involves Transcranial Magnetic Stimulation (TMS). The goal of the study is to understand how different brain areas contribute to different aspects of music perception. Participants will be compensated for their time. For more information, please contact the Grahn Lab TMS e-mail at neuromusicTMS@gmail.com. Be sure to include your name and phone number where you can be contacted. Unfortunately we **cannot** accept anyone who: is hearing impaired, has a pacemaker or any metal implants in their body, has blackouts or has had seizures, has claustrophobia, is pregnant, and has piercings that cannot be removed. Safety screening will be conducted prior to TMS.

Neuroscience of Music Study
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APPENDIX B

PARTICIPANT SCREENING FORM FOR TMS

The Effects of Transcranial Magnetic Stimulation on Auditory Rhythm and Beat Perception

ID Code: ______________________
Date: ______________________
Date of Birth: ______________________
Handedness: right/ left/ mixed

	YES	NO
Have you previously had an MRI or fMRI scan?		

	YES	NO
Have you ever had surgery? Type:______________________		
Have you ever been injured by a metallic foreign body which was not removed (e.g., bullet, BB, shrapnel)?		
Have you ever worked with metal (grinding, fabricating, welding, etc.) or ever had an injury to the eye involving a metallic object (e.g., metallic slivers, shavings)?		
Do you have a cardiac pacemaker or defibrillator?		
Do you have severe heart disease (including susceptibility to arrhythmias)?		
Do you have an aneurysm clip?		
Do you have cochlear (ear) implants?		
Do you have Meniere's disease?		
Do you have dental work other than fillings? Type:______________________		
Do you have any tattoos or permanent eyeliner?		
Do you have any body piercings that cannot be removed?		
Do you wear a hearing aid or false teeth?		
Have you ever experienced claustrophobia or a panic attack?		
Have you ever had an epileptic seizure?		
Is there a history of epilepsy in your family?		
Have you ever had a head injury?		
Have you had any visual disorders?		
Do you get migraines and / or are susceptible to headaches?		
FOR WOMEN ONLY:		
Are you pregnant, experiencing a late menstrual period, or at risk of conceiving (i.e., sexually active and not using a reliable form of birth control)?		
Are you breast feeding?		
Do you have an intrauterine device (IUD)?		
Are you wearing an underwire bra?		

PLEASE REMOVE THE FOLLOWING	CHECK
Any jewellery	
Any body piercings	
Your wristwatch	
Any hair pins or barrettes	
Your wallet and credit cards	
Everything from your pockets	

APPENDIX C

LETTER OF INFORMATION FOR PARTICIPANTS

The Effects of Transcranial Magnetic Stimulation on Auditory Rhythm and Beat Perception

Principal Investigator:
Jessica Grahn, Ph.D.
Brain and Mind Institute
Room 229, Natural Sciences Building
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London, Ontario, N6A 5B7
Email: jgrahn@uwo.ca
Phone: 519-661-2111 x84804

Introduction:

You are invited to voluntarily participate in a research study investigating the role of brain areas known to contribute to the perception of rhythm and beat in music, using transcranial magnetic stimulation, or TMS. The purpose of this study is to determine how specific brain regions may be responsible for different aspect of musical perception and experience. This letter of information will provide you with further information about behavioural tasks and techniques that will be used during the experiment allowing you to make an informed decision regarding participation in this research.

Research Procedures:

If you agree to participate in this study, your participation will involve behavioural tasks that include:

Rhythm/ Beat Perception Tasks:

During the study, you will hear stimuli that fall into three categories: metronomic/ isochronous beeps, metric or non-metric rhythms, and music clips (e.g. clips from recorded musicians). Tasks fall into four categories: discrimination, passive listening, beat-tapping, and reproduction tasks. You will hear stimuli and may be asked to simply listen passively, or to make perceptual judgments about the sounds, and/or make responses to the sounds. If the task is complex, you will be given a chance to practice before the session begins. You may be completing these tasks before and after TMS is applied to the scalp (offline TMS), or at the same time as TMS is applied (online TMS). Overall, these experiments will inform us about the role of different brain areas in music processing.

Transcranial Magnetic Stimulation (TMS):

TMS allows scientists to stimulate the brain non-invasively by a rapid switching of a current in a coil placed over the head. When triggered, the capacitors send an electrical current through the coil resulting in the generation of a magnetic field. Placed over the head, the magnetic field passes through the scalp and induces a physiological current, which in turn temporarily affects neural activity in the brain. The procedure is painless because the magnetic field passes through the scalp and skull freely. Activation of the magnetic coil produces a ‘clicking’ noise. You will wear headphones to protect your hearing. You may undergo two forms of TMS: “single-pulse TMS” and “high-frequency repetitive TMS”. “Single-pulse TMS” involves placing the magnetic coil over your scalp

 Participant’s Initials: _______

APPENDIX D

Western
The Brain and Mind Institute

If YES, please elaborate: ______________________________

____

8. Have you ever had any other brain-related condition?
(YES/NO)
If YES, please elaborate: ______________________________

____

9. Have you ever had any illness that caused brain injury?
(YES/NO)
If YES, please elaborate: ______________________________

____

10. Are you taking any medication (YES/NO), including:
a) Prescription medication (including but not limited to antidepressants, antipsychotics, antibiotics)? (YES/NO)
b) Over-the-counter drugs or herbal remedies? (YES/NO)
c) Street/Recreational drugs (i.e., cocaine, ecstasy, etc.)? (YES/NO)

Have you consumed any alcohol in the past 24 hours? (YES/NO)

Are you experiencing any alcohol or drug withdrawal symptoms? (YES/NO)

If you answered YES to any questions about drug and alcohol use, please elaborate:

____

____

11. If you are a woman of childbearing age, are you sexually active, and if so, are you *NOT* using a reliable method of birth control?
(YES/NO)
If YES, please elaborate: ______________________________

____

12. Does anyone in your family have epilepsy?
(YES/NO)
If YES, please elaborate: ______________________________

____

13. Do you need further explanation of TMS and its associated risks?
(YES/NO)
If YES, please elaborate: ______________________________

____