THE RHYTHM NETWORK: AN ACTIVATION AND FUNCTIONAL
CONNECTIVITY ANALYSIS OF BEAT PERCEPTION AND
PRODUCTION

A Thesis
Presented to the
Faculty of
San Diego State University

In Partial Fulfillment
of the Requirements for the Degree
Master of Arts
in
Interdisciplinary Studies

by
Dane E. Anderson
Fall 2013
SAN DIEGO STATE UNIVERSITY

The undersigned Faculty Committee Approves the

Thesis of Dane E. Anderson:

The Rhythm Network: An Activation and Functional Connectivity Analysis of
Beat Perception and Production

Ralph-Axel Müller, Chair
Department of Psychology

Joseph M. Waters
School of Music and Dance

Henrike K. Blumenfeld
School of Speech Language and Hearing Sciences

John Iverson
Swartz Center for Computational Neuroscience, UC San Diego

August 6th, 2013
Approval Date
ABSTRACT OF THE THESIS

The Rhythm Network: An Activation and Functional Connectivity Analysis of Beat Perception and Production
by
Dane E. Anderson
Master of Arts in Interdisciplinary Studies
San Diego State University, 2013

The perception of beat, while seeming easy and intuitive, is a rather complex cognitive and sensorimotor achievement that at times can manifest as a visceral sensation. Deficits in beat perception also appear to positively correlate with increased impairment in movement disorders such as Parkinson’s disease. Neuroimaging has shown findings like these are likely due to rhythm perception and production relying on a complex interaction of auditory and motor regions, in association with a supportive network that includes prefrontal, parietal, and deep striatal areas of the brain. This study therefore aimed (I) to use traditional task-based activation techniques (fMRI) to define the critical regions of the rhythm network under both a beat rating (BR) and beat production/maintenance (BPM) cognitive task; and (II) employ task-based functional connectivity (fcMRI) methods, to map the most important connections within this network, highlighting how they may change dependent on task behavior and stimuli. Activation results for 14 normal right-handed participants (4F : 10M, 24 yrs ± 4.54) confirmed much of the current literature and indicated that both beat perception and production recruit neural resources from predominantly overlapping regions of a single network. Functional connectivity analyses described a network whose connectivity is relatively stable regardless of stimuli or task. Differences between perception and production of rhythm appear to stem from specific, subtle changes in the synchronicity between particular regions. To our knowledge, the correlation matrices and connectivity maps derived from our fMRI-fcMRI data are the first comprehensive representations of the rhythm network as a whole.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT ................................................................. iv</td>
</tr>
<tr>
<td>LIST OF TABLES ............................... vi</td>
</tr>
<tr>
<td>LIST OF FIGURES ................................ vii</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS ......................... viii</td>
</tr>
<tr>
<td>CHAPTER</td>
</tr>
<tr>
<td>1 INTRODUCTION ........................................... 1</td>
</tr>
<tr>
<td>Magnetic Resonance Imaging .......... 2</td>
</tr>
<tr>
<td>The Rhythm Network ...................... 3</td>
</tr>
<tr>
<td>2 METHODS ............................................... 6</td>
</tr>
<tr>
<td>Protocol &amp; Participants ................ 6</td>
</tr>
<tr>
<td>Stimuli &amp; Tasks .............................. 7</td>
</tr>
<tr>
<td>Task 1 (Beat Rating [BR]) ............... 9</td>
</tr>
<tr>
<td>Task 2 (Beat Production/Maintenance [BPM]) .......... 9</td>
</tr>
<tr>
<td>Image Acquisition ....................... 10</td>
</tr>
<tr>
<td>Analysis ............................................. 10</td>
</tr>
<tr>
<td>3 RESULTS .............................................. 14</td>
</tr>
<tr>
<td>Behavioral ......................................... 14</td>
</tr>
<tr>
<td>Activation .......................................... 14</td>
</tr>
<tr>
<td>Connectivity ...................................... 16</td>
</tr>
<tr>
<td>4 DISCUSSION ......................................... 22</td>
</tr>
<tr>
<td>Limitations &amp; Future Directions ........ 25</td>
</tr>
<tr>
<td>Conclusion ........................................... 25</td>
</tr>
<tr>
<td>REFERENCES ......................................... 27</td>
</tr>
<tr>
<td>APPENDIX</td>
</tr>
<tr>
<td>ROI TABLE ............................................. 31</td>
</tr>
</tbody>
</table>
LIST OF TABLES

Table 1. Listing of Regions of Interest (ROIs) Utilized for Within Network Analyses. Clusters Determined via Use of Variable Thresh-Holding of Task 1 (SM > Null) Activation Contrast, and “Cluster to Whole-Brain” Analyses. ..........................32
LIST OF FIGURES

Figure 1. Graphic and formal musical notation representation of P&E pattern [311211214]. .................................................................7

Figure 2. Diagram of SM stimulus trial. The “Auditory Stimulus” is composed of three strong “clock-inducing” patterns, with tones indicated by red bars. .................8

Figure 3. Cluster to whole-brain functional connectivity (Wb FC) analyses for left anterior cerebellum(*) and left D/VLPFC(**). ................................................13

Figure 4. A. Graph of average response for SM and NM stimuli. * (p<.001) B. Graph of average BR accuracy for SM and NM stimuli. * (p<.001) C. Graph of average BPM %deviation for SM and NM stimuli. * (p=.041) .....................................14

Figure 5. Beat Rating (BR) task, strongly metrical – null stimuli. Significance thresholding at p < .01. .................................................................................................15

Figure 6. Selected slices from Beat Rating (BR) task activation contrast of strongly metrical (SM) – non-metrical (NM stimuli. (p<.05) ..................................................16

Figure 7. Beat perception and maintenance (BPM) task contrast of strongly metrical – null stimuli. (p<.05) .................................................................................................17

Figure 8. Selected slices from Beat production and maintenance (BPM) task activation contrast of strongly metrical versus non-metrical stimuli. (p<.05) ..........17

Figure 9. Comparison of Beat rating (BR) and Beat perception and maintenance (BPM) task’s strongly metrical vs. Null stimuli. (p<.05) .............................................18

Figure 10. Correlation Matrices for BR(a) and BPM(b) tasks. ......................................................19

Figure 11. A graphical representation of those ROI pairings with the highest (> .065) correlation coefficients for strongly metrical (SM) stimuli in either cognitive task. (p<.01). .................................21
ACKNOWLEDGEMENTS

Without the facilities and support of Dr. Ralph-Axel Müller of the Brain Imaging Development Lab neither this degree program nor this research project would have gotten off the ground, and thus great appreciation is extended to him here. Within the BDIL the invaluable impact Chris Keown’s patient assistance and troubleshooting cannot be stressed enough, and I thank him with deepest sincerity for all his time and effort.

The original idea and data for the study were gracious gifts of Dr.’s John Iversen and Daniel Callen. I can only hope the work produced here is worthy of their trust and support.

Last and most importantly, for the decades of endless support, guidance, and love I must thank my parents. I will never be able to put in words what you two are, and have done for me.
CHAPTER 1

INTRODUCTION

To most individuals a song’s “beat” is a series of rather finite moments where the rhythm dictates a note should be placed. A well-trained musician however would likely not describe fleeting moments, but wide expanses of time and space. For although “beat” is often defined as a perceived pulse occurring at equal intervals (Cooper & Meyer, 1960), people are rarely conscious of subtle changes in those intervals over time. Our musician might therefore explain how one can play at the earliest onset of the beat to “push the tempo,” or hold way back along trailing edge and play “in the pocket”. So how is it both feel on the beat? And why does that perception of rhythm seem to manifest as a visceral feeling in the body, often requiring one to tap along in order to find where the correct beat is? 

Besides how fluid the human sense of time can be (Angrilli, Cherubini, Pavese, & Manfredini, 1997; Droit-Volet, & Meck, 2007; Schiffman & Bobko, 1974), the answer most likely lies in understanding the perception of rhythm depends on not only on the auditory system but also several different motor regions of the brain (Chen et al., 2008a, 2008b; Grahn, 2009; Grahn & Brett, 2007; Zatorre, Chen, & Penhune, 2007) and thus may centrally involve an embodied visceral component. Neuroimaging studies have gone on to show both beat perception and beat production utilize not only those auditory and motor regions, but an elaborate network which also includes, prefrontal, parietal, and deep striatal areas of the brain (Grahn & Rowe, 2013; Kung, Chen, Zatorre, & Penhune, 2013; McAuley, Henry, & Tkach, 2012). The involvement of such a wide distribution of neural regions is quite logical given that, despite feeling easy and intuitive, both rhythm perception and production are rather complex cognitive achievements involving directed attention, auditory discrimination, temporal prediction, rapid error detection, response inhibition and finely controlled motor abilities. Some researchers speculate that it may actually be the interactions between brain regions which generate these abilities, rather than the specific regions themselves (McAngus, O’Boyle, & Lee, 1999). Close examination of this rhythm network and how its component areas interact is therefore essential to understanding these phenomena.
Unraveling the complex neural relationships underlying beat perception is a worthy scientific goal all on its own. However, it may also be a critical step towards understanding a group of debilitating disorders and improving future treatments. Recent research has tied deficits in beat perception to increased symptom severity in dyslexia (Huss, Verney, Fosker, Mead, & Goswami, 2011; Thomson & Goswami, 2008), certain types of aphasia (Szelag, von Steinbüchel, & Pöppel, 1997; Tomaino, 2012), and Parkinson’s disease (Grahn & Brett, 2009; Pastor, Artieda, Jahanshani, & Obeso, 1992). Perhaps more importantly, rhythmic stimuli are proving to be efficacious interventions for some of these disorders. Several remarkable studies have demonstrated external rhythms can assist in reducing stutters (Adams & Hotchkiss, 1973; Brady, 1969; Hanna & Morris, 1977), and coordinating gait of those with serious movement disorders such as Parkinson’s (McIntosh, Brown, Rice, & Thaut, 1997; Rochester et al., 2005; Roerdink, Bank, Peper, & Beek, 2011).

The current study therefore attempts to incorporate converging functional magnetic resonance imaging (fMRI) techniques to map the neural correlates of beat perception, along with the connectivity between those regions. Specifically we aim (I) to use traditional task-based activation techniques (fMRI) to replicate existent findings and define the critical regions of the network under both a beat rating (BR) and beat production/maintenance (BPM) task; and (II) employ task-based functional connectivity (fcMRI) methods, to map the most important connections within this network, highlighting how they may change dependent on task behavior and stimuli.

**MAGNETIC RESONANCE IMAGING**

fMRI technology is based the ferromagnetic nature of deoxygenated human hemoglobin. This trait enables researchers to track cerebral bloodflow over time as it travels away from recently employed or “activated” neural tissues. By comparing regular measurements of the blood oxygen level dependent (BOLD) signal within each 3D volumetric unit (voxel) of the brain, under both a behavioral and baseline condition, it is possible to isolate what regions on average used significantly more blood during a behavior. fcMRI employs the same BOLD signals but assesses not their overall regional strength, but rather the correlational relationship between separate areas’ signals over time. In this way one can locate regions of the brain whose temporal activity are closely related, and therefore
likely to have been reacting similarly to a given stimuli, or interacting with one another in such a way as to be functionally “connected” or “co-activating”.

**THE RHYTHM NETWORK**

The neural correlates of beat perception and production can be loosely grouped in three functional categories: Auditory, Motor, and Varied. The Auditory region most commonly seen in activation analyses are the primary auditory cortices (PACs) including Heschl’s gyri, located along the Sylvian fissure (lateral sulcus) of the superior temporal gyri (Grahn & Brett, 2007; Liégeois-Chauvel, Peretz, Babaï, Laguitton, & Chauvel, 1998; Zatorre et al., 2007). These homologous though somewhat functionally differentiated regions are commonly active during auditory tasks as they are associated with first order processing of sound in the brain (Penhune, Zatorre, & Feindel, 1999; Specht & Reul 2003; Zatorre, Belin, & Penhune, 2002).

The Motor regions seen activating in response to rhythmic stimuli on the other hand typically include the putamen (Grahn & Rowe, 2009), supplementary motor areas (SMAs) (Grahn & Brett, 2007), and various portions of the cerebellum (Chen, Zatorre, & Penhune, 2006; Zatorre et al., 2007). The putamen, as part of the basal ganglia, is tied significantly to the initiation and coordination of gross motor functions, while the cerebellum is most typically responsible for fine motor control (Zatorre et al., 2007). Deterioration of striatal tissues is in fact one of the strongest biological links we have between Parkinson’s disease and deficits in beat perception (Bruck et al., 2001; Grahn & Brett, 2009). The SMA, located within the precentral gyrus, is most typically considered a planning area for motor commands and organizes sequences of movements (Lee & Quessy 2003; Roland, Larsen, Lassen, & Skinhoj, 1980). It is one of the areas (along with the cerebellum) researchers were surprised to see active in totally stationary participants listening to rhythmic stimuli. Though the cerebellum is one of the main motor, coordination and learning regions of the brain, more recent work has shown activation in the area also correlates strongly with internal timing tasks (Harrington, Lee, Boyd, Rapcsk, & Knight, 2004; Teki, Grube, Kumar, & Griffiths, 2012). This may indicate similar regions may be coopted or shared between timing abilities and the perception of beat (Teki et al., 2012), and lends support to our hypothesis of a rhythm network which perhaps overlays with a timing network.
The Variable regions implicated in beat perception either play multiple roles within the network or researchers are as of yet unsure of their function. These areas typically include the thalamus and dorsal/ventral lateral prefrontal cortex (D/VLPFC). The thalamus for example is the major routing center of almost all stimuli and signals (including auditory and motor) to and from the brain (Jones, 1991). From an auditory pathway perspective one might expect it is the medial geniculate nucleus activating within the thalamus as the pathway of sound stimuli from the auditory brainstem to the auditory cortical regions. Alternatively the thalamus could be acting as a motor region via the ventral lateral geniculate nucleus, as that sub-region generally conducts movement signals between the brain and body (Jones, 1991). It is as of yet unclear which is the case, if not both. That being said, our FC analyses indicated a strong coupling between the thalamus and the basal ganglia rather than the PACs during both the beat perception and production tasks (Results Sec.). The least understood region classically linked to rhythmic tasks is the D/VLPFC (Chen et al., 2006; Kung et. al., 2013; Zatorre et al., 2007). Decades of work have linked this area to judgment, decision making, inhibitory functions, working memory, attention, semantic knowledge, language, abstract thinking and mood. Other work has shown it may coordinate with the premotor cortex, and have motor planning and regulatory functions (Abe & Hanakawa, 2009), a finding which could account for its activation during beat perception tasks, although response inhibition and attention are also options. That being said, the frontal and prefrontal areas represent the highest, most complex executive regions of the cerebral cortex, and the scientific community still knows comparatively little about them. Thus we cannot definitively say how the region is contributing to the rhythm network.

To the best of our knowledge, there have been only a few research groups who have used FC techniques to investigate connections between these regions. These researchers have mostly employed psychophysiological interaction (PPI) analyses, seed to whole-brain FC analyses, or a combined version of the two. Thus far all work has utilized only a single region or a small subset of areas, as seeds (small spherical voxel regions), to conduct analyses. Most recently, Kung and colleagues (2013) used such a combined analysis to look at which regions correlated most strongly with the right superior temporal gyrus (STG) and VLPFC, and how that connection modulated depending on strong vs. weakly metrical stimuli. They found the two seeds showed stimulus modulated coupling with both the
premotor cortex (PMC) and inferior parietal lobule (IPL). More specifically the VLPFC showed coupling to “the right DLPFC and bilateral BG [basal ganglia] at the border of the caudate and putamen” (Kung et al., 2013). Grahn and Rowe (2009) utilized PPI analyses between spherical seeds in the bilateral putamen, STGs, SMAs, PMCs and the cerebellum to assess how the coupling varied between duration vs. volume accented, and beat vs. non-beat rhythmic stimuli. Results indicated beat vs. non-beat stimuli modulated connectivity between putamen and the PMCs, SMAs, and right STG, with a strong but non-significant similar trend with the left STG and cerebellum. Connections were also found between the anterior portion of the putamen and the bilateral PMCs and cerebellum. A follow up group of analyses on the SMA and PMC found modulating connectivity between each seed, its laterally homologous region, the subsequent bilateral ROI, and the STGs (Grahn & Rowe, 2009). In 2008a Chen, Penhune, et al. and in 2006 Chen, utilized two different FC analyses on a beat production task. In the earlier study a PPI analysis determined seeds in both the dorsal premotor cortex (DPMC) and planum temporale (PT)/STGs correlated and modulated and depending on accented vs. unaccented stimuli (Chen et al., 2006). The second study utilized a combination whole-brain approach with similar initial seed in the DPMC to identify what areas correlated most strongly throughout the brain. They found significant voxels during their tapping task in the pre-SMA, PMC, DLPFC, IPL, precuneus, anterior insula, thalamus, and anterior cerebellum (Chen et al., 2008a).

In comparison to this past work, our study not only examined the neural regions underlying both beat perception and beat production, but compared the two behaviors: beat perception without moving, and with tapping the beat. Moreover, we employed a two-pronged FC analysis approach, incorporating not a subset, but all identified essential beat perception ROIs, in an effort to present a more comprehensive view of the network and its internal connections.
CHAPTER 2

METHODS

PROTOCOL & PARTICIPANTS

Eighteen right-handed individuals were recruited by Dr. Daniel Callen’s research team, from the Kyoto, Japan area to participate in two beat perception tasks during fMRI scanning at ATR laboratories. Upon entering the laboratory and providing informed consent these participants underwent structured interviews concerning their medical history and background. Individuals whose responses might preclude a safe MRI scan (eg. metal implants, history of claustrophobia, potential pregnancy etc.), or indicated hearing impairment, formal and/or current musical training (>3 years), or the presence of neurological disorders were not enrolled in the study. Next, accepted participants completed a short practice trial with stimuli similar to the experimental tasks to determine if they could reliably detect when a strongly metrical rhythm was present, versus when it was not. “Strongly metrical” (SM) was operationally defined as eliciting the perception of a defined pulse whose intervals are equivalent and can be hierarchically structured. Informally, they are stimuli with a strong sense of beat that would be easy to tap your foot to. Participants whose responses did not show a statistically significant difference ($p < .05$) between average ratings of SM stimuli and those of contrasting stimuli without a strong sense of beat, did not continue onto scanning. All other participants proceeded to undertaking the experimental protocol during fMRI scanning.

Initial pre-processing of data revealed four participants who either did not follow task directions adequately or had excessive movement artifacts and were therefore removed from further analyses. Therefore 14 participants (4F : 10M, 24 yrs ± 4.54) provided data for the primary beat rating task. A fifth individual’s datum was excluded from the secondary task due to movement artifacts within those scans. Thus only 13 participants (4F : 9M, 23.85 yrs ± 4.69) were analyzed in the secondary beat production/maintenance task.
STIMULI & TASKS

The auditory stimuli for both tasks were broken into three categories:

A. Strongly Metrical (SM)
B. Non-Metrical (NM)
C. Null/Silence

The tone sequences presented in these stimuli were based on temporal patterns taken from Povel and Essens (1985) who investigated perceptions of different rhythmic patterns, which were all permutations of nine basic inter-onset-intervals (IOIs) contained in the set “1 1 1 1 2 2 3 4”. In this nomenclature the integers represent a multiple of a standardized duration set to follow a single tone (Figure 1).


The top 15 “clock-inducing patterns,” from the Povel and Essens (1985) study - or those IOI sets that most strongly generate an internal clock-like pulse - were randomly organized into 30 rhythmic stimuli, each a combination of three patterns. These combined pattern sets were then randomly assigned one of five tempi (180, 190, 200, 210, or 220ms) as their IOI in order to generate 30 Strongly Metrical (SM) stimuli. Each experimental stimulus was therefore composed of a different pattern of 27 tones, and lasted between ~8.5 and 10.5 seconds depending on assigned tempo (Figure 2). All tones were identical (500Hz sine wave, 70ms duration, with a rise/fall of 8ms) to take advantage of the cognitive phenomenon known as “subjective accenting,” where one perceives “ticks” vs. “tocks” in metrically significant locations despite stimuli being identical. Research groups have shown it is quite
common for participants to unconsciously modulate early auditory perceptions of rhythms in this way (Povel & Okkerman, 1981; Repp, 2007; Repp, Iverson, & Patel, 2008). Iversen et al., (2009), among others, have shown this “endogenous metrical interpretation of ambiguous stimuli” can be seen occurring in the neural correlates of beat perception (Brochard, Abecasis, Porter, Ragot, & Drake, 2003; Snyder & Large, 2005). Work done by Grahn & Rowe (2009) has shown relative to both volume and duration accented stimuli, unaccented significantly increase BOLD activation in the basal ganglia. Thus it was hypothesized requiring participants generate their own subjective metrical structures for unaccented stimuli would activate beat perception areas more robustly than if exogenous accents were provided.

Non-Metrical (NM) stimuli were generated via randomizing the 27 P&E integers within each SM composite pattern. These new rhythms were then randomly assigned one of the same five tempi used to generate the SM stimuli. While these new patterns involved the same integer ratios, some still falling at appropriate metrical locations, pilot data showed they no longer evoked a sustained sense of beat, and were consistently rated as being without Therefore they were labeled Non-Metrical (NM). Importantly each file in both conditions had a combination of 1.5 – 4.5sec of silent response and jitter appended to the tone segment such that each file was between 12 and 13 seconds in length (Figure 2).
The Null stimuli were 30 audio files of silence the same duration as SM and NM stimuli. Though Null stimuli contained no sound, null periods of course involved scanner noise for participants during the protocol. However, they were provided with earplugs and all stimuli were presented via over-ear, noise-blocking headphones to keep interference to a minimum. We feel the high task performance clearly indicated scanner noise did not interfere with the task (see Behavioral Results).

**Task 1 (Beat Rating [BR])**

Participants were presented with 30 randomized auditory stimuli (10 SM, 10 NM and 10 Null) in each of six back-to-back trials, and asked to “*Indicate how strongly you felt the beat of each audio event was once it finished playing.*” Their ratings of the 180 total auditory events were recorded via a four-button response box where from left to right:

- Button “1” indicated strong certainty of NO beat,
- Button “2” moderate certainty of NO beat,
- Button “3” moderate certainty there was a beat, and
- Button “4” strong certainty there was a beat.

During Null stimuli participants were instructed to randomly choose a rating so that an aural/motor response baseline could be utilized in later subtractive analyses.

**Task 2 (Beat Production/Maintenance [BPM])**

Participants were presented with newly randomized batches of 30 auditory stimuli (10 SM, 10 NM and 10 Null) pulled from the same audio files utilized in BR Task 1. Over three back-to-back scans participants were asked to “*Tap along with what you felt is the underlying beat as soon as you were able,*” continuing till the onset of the next stimulus. During the Null stimuli (hence to be referred to as NullTap events for BPM) participants were instructed to tap any steady beat which came to them. Taps were recorded via the same response box as task 1, and participants were asked to choose a preferred button to use for the length of the task.

Since P&E clock-inducing patterns were employed in creating all stimuli, metrical rhythms were naturally generated. However, this did not mean a tone was heard at all metrically expected points, even if participants were tapping at the appropriate beat locations. A certain degree of low-level syncopation was present in SM stimuli, and to a much greater
degree in the NM. The additional 1.5 – 4.5 sec of response and jitter at the end of each auditory file (Figure 2) also meant participants would continue tapping for several unassisted seconds before the next audio event. For both these reasons we considered Task 2 both a beat production and beat maintenance task, rather than one of synchronization.

**IMAGE ACQUISITION**

Participant’s anatomical and functional data were acquired using a 3T Siemens Tim Trio fMRI imagining system, with a standard eight channel head coil. After standard head position localizers, a high-resolution (1x1x1mm) fast spoiled gradient echo (FSPGR) T1-weighted anatomical image was collected for anatomic localization and co-registration. Nine echo planar (EPI) T2*-weighted blood oxygenation level dependent (BOLD) signal functional scans followed. Each 2500ms imaging volume encompassed 40 slices (TE = 30ms, Image matrix = 64 x 64, 4x4x4mm resolution, FOV = 17.92 x 17.92cm, Flip angle = 80°) covering the whole brain and cerebellum.

**ANALYSIS**

Behavioral: For the BR Task, responses indicating No Beat and Beat, were combined across certainty ratings (strong and moderate) and scored as correct or incorrect in concordance with the particular audio file they referenced. Accuracy was then calculated as a percentage (correct responses/total responses) for SM stimuli and NM stimuli. One-sample level t-test at both the participant and group level were performed to ensure results were above chance. Group level t-testing between participant’s average ratings of SM and NM stimuli confirmed whether on average they were able to correctly discriminate between the presence and lack of beat.

Determining BPM Task accuracy required calculating the mean Inter-tap-Interval (ITI) across all taps performed during a single stimulus event. Instances where participants tapped twice inside ½ a stimuli’s Inter-beat Interval (IBI) - four times the stimuli’s tempo - were assumed to be accidental “double taps” and secondary taps were therefore removed. Both ITI and percent Deviation (%dev) are used in the literature as measures of period matching, and the ability to reproduce time intervals between sequential events (Chen et al.,...
2008b; Patel, Iverson, Chen, & Repp, 2005; Repp, 2010). Mean %dev was calculated across participant for SM and NM stimuli so that a two-sample t-test could determine if, on average, participants successfully found and maintained the correct beat. It was noted that several participants had particularly high %dev scores -around 50%- on many trials. Examination showed these participants had a tendency to tap at a higher subdivision of the beat, along what might be considered eighth rather then quarter notes. Therefore to ensure %dev scores correctly represented their accuracy, IBIs of those particular trials were halved to match their higher tapping rates.

Activation: Processing and analysis of all imaging data was undertaken using the AFNI software system (Cox, 1996). Anatomical and functional scans were co-registered to one another, skull-stripped, and normalized to standard Talairach stereotaxic space (Talairach & Tournoux, 1988). EPI functional scans had the first two image volumes removed and the subsequent volumes de-trended (removal of very low frequency temporal variation) and realigned to the third volume. Head motion was summed across three translational axes, and three rotation vectors. Any shift greater than 0.3mm was auto-censored via scripts. All data were also inspected visually, volume by volume, for any motion artifacts missed at prior stages. Once complete BOLD signal was scaled and smoothed with a 6mm full width at half maximum (FWHM) isotropic Gaussian kernel. Statistical data analysis applied a general linear modeling approach where motion (<0.3mm) and task condition onsets/durations were modeled as regressors in order to have their effects removed, along with probable error. This was performed using AFNI’s 3dDeconvolve program where the linear model is fit to the preprocessed fMRI time series to solve the necessary parameter estimates, utilizing standard least squares methods; ultimately generating the estimates of effects, standard error, and statistics for the relevant planned contrasts both between and within participants. All results were then cluster corrected ($p < .05$) for multiple comparisons.

The initial planned contrasts utilized the Null stimuli as baseline (eg. SM > Null and NM > Null), to determine areas active during beat perception and production. Analysis of SM > NM contrast would locate brain regions whose activation was greater for strongly metrical as compared to non-metrical rhythms, and thus may be part of a beat-processing network. To determine whether production and maintenance of beat utilizes different neural regions than perception, a paired sample t-test was conducted between tasks. To prevent false
positives arising from subtracting voxels with negative effects of one contrast from those of another [ie. \((SM > Null)_{BR} vs. (SM > NullTap)_{BPM}\), masked versions of each (positive and negative) were created and compared separately.

Connectivity: All imaging volumes for functional connectivity (FC) analyses were pre-processed in the same manner as the activation data. Network nodes, or regions of interest (ROIs), for analyses were generated from the activation analysis, confirmed and expanded via cluster to whole-brain correlational analyses, then checked against the literature. We opted for a functional, cluster-based approach, rather than an anatomical, seed-based one, with the aim of enhancing the task specific signal generated for each region.

ROI clusters were defined as ~27 contiguous voxels of highest activation within a given area of the SM > Null task 1 contrast. For smaller anatomical regions (e.g. thalamus, putamen and caudate) the target goal was ~14 voxels.

To ensure no important areas were overlooked because they did not appear significantly active via contrast, average time series from existent ROIs were employed in individual correlation analyses with all voxels in the brain (Figure 3). This “ROI to whole-brain” FC analysis allowed us to ascertain whether, based on a significantly correlated BOLD signal, any other regions were co-activating or “synchronizing” with a given ROI, and therefore likely involved in similar or related neural processes. Cluster correction was utilized to account for issues of multiple comparisons across the brain. For our purposes if at least two of these whole-brain ROI analyses indicated an additional anatomical region had high BOLD correlation it was added to the network list. The inclusion of clusters in left posterior cerebellum, the caudate and the inferior parietal lobe (Figure 3) occurred in this manner. The final list of 18 ROIs (9 ROIs in each hemisphere) employed in the subsequent FC analyses can be found in Table 1 in the Appendix. As mentioned, all areas were then checked against findings in the literature. All areas produced via this process were consistent with the literature, and no completely novel regions were found to be associated with beat perception or production.

Next, correlation matrices were created for each task’s SM and NM conditions, to ascertain which ROI pair’s connectivity significantly varied depending on beat. Unlike the broader cluster to whole-brain analyses, these matrices focus solely on ROI clusters and
allow direct comparisons between ROI interconnectivity measures across different conditions and tasks. Hence such matrices provide one of the first representations of the beat network as a whole. Overall network connectivity was compared in both tasks via a paired sample t-test of average correlation strength during SM vs. NM stimuli. To investigate whether connectivity between specific regions varied depending on beat strength of stimuli, the average correlation coefficient of each ROI pairings during each stimuli (SM vs. NM) were run through a one-tailed paired sample t-test.

Finally, in an effort to provide a better visualization of the network, the strongest network connections for the SM condition were presented graphically, with connections visually weighted by relative correlation strength, for both BR and BPM tasks. While the literature does not provide any guidance for determining an appropriate threshold for functionally important connections, the strongest 1/3, or connections with coefficients >0.66 were chosen here for presentation. This correlation strength is consistent with connections significant above \( p < .01 \) in a one same t-test. We feel such “maps” will be important for developing clearer impressions of how the network may be laid out, and be integral to inspiring future work in the area.
CHAPTER 3

RESULTS

BEHAVIORAL

In the primary BR task where participants were asked to rate the strength of the beat, participants performed significantly greater than chance on both SM ($p<.001$) and NM stimuli ($p<.001$) in fact accuracy for both stimuli were above 90% (Figure 4b). More importantly, the two sample t-tests between average response for SM vs. NM showed participants could easily discriminate between stimuli with a strongly metrical pulse vs. those without ($p<.001$) (Figure 4a).

Figure 4. A. Graph of average response for SM and NM stimuli. * ($p<.001$) B. Graph of average BR accuracy for SM and NM stimuli. * ($p<.001$) C. Graph of average BPM %deviation for SM and NM stimuli. * ($p=.041$)

During the BPM task, participants found it on average significantly more difficult ($p=.041$) to tap and maintain the beat during NM stimuli (4.03 %dev) as compared to SM (0.25 %dev) (Figure 4c). Considering performance on both tasks was extremely high with little variance across subjects, we feel any doubts concerning rhythmic scanner noise having interfered with, or altered performance can be put aside.

ACTIVATION

Overall in both tasks it was found the SM condition correlated with increased activation of expected beat perception regions relative to NM and Null/NullTap conditions. Specifically, during the BR task when comparing SM to Null conditions (see Figure 5),
participants on average showed significant, cluster corrected, activation ($p<.01$) in the bilateral primary auditory cortices (PACs), dorsal/ventrolateral prefrontal cortices (D/VLPFCs), supplementary motor areas (SMAs), inferior parietal lobules (IPLs), anterior cerebellum (VI/V), and the right posterior cerebellum (VI/V). There was also significant activation in the basal ganglia, including putamen and caudate nuclei, the bilateral thalami, and the brain stem. It should be noted that Figure 5 shows inverse effects (stronger BOLD signal for Null as compared to SM, shown as blue regions in Figure 5 were detected in both anterior cingulate cortex (ACC), precuneus, the parietal lobes. These inverse effects were found in both SM > Null and NM > Null contrasts. When comparing NM > Null the activation was extremely similar though perhaps less robust. This difference was confirmed in the SM > NM contrast which only showed stronger activation within the putamen, and the anterior cingulate cortices (ACC) and precuneus (see Figure 6).
In the secondary BPM task, the SM > NullTap contrast showed significant activation ($p<.05$) only in a subset of those areas seen in BR (see Figure 7). The areas, which correlated strongly with rhythmic stimuli, included bilateral PACs, D/VLPFCs, SMAs with no difference in the activation of the basal ganglia or thalamus. However there was higher BOLD signal seen far forward in the right inferior frontal gyrus (IFG), which was not present in BR. Comparison of NM > NullTap showed a similarly reduced activation pattern as SM with activation of bilateral PACs, D/VLPFC and SMAs. Interestingly NM stimuli seemed to be associated with activity in both right and left IFG as well as the right IPL. The only differences found in the SM > NM contrast were significantly greater BOLD response ($p<.05$) in the left putamen and thalamus for SM stimuli, and in right IFG for NM stimuli (See Figure 8).

When performing a direct pairwise comparison of BR and BPM tasks, i.e. [(SM > Null)BR vs. (SM > NullTap)BPM] the results confirmed the general differences noted above. BR has significantly higher activation in the bilateral PACs, D/VLFPCs, SMAs, right cerebellum and the putamen (Figure 9). BPM on the other hand seems to have stronger BOLD responses in cingulate cortex and precuneus. Initially it was thought this result was derived from default mode network response mentioned previously, however equivalent Null time-series were used in each task’s contrast and should have mostly removed any such findings. That a similar anterior cingulate cortex (ACC) was seen between SM and NM stimuli in the BR task lends credence to the finding.

**CONNECTIVITY**

Functional connectivity analyses showed a densely interconnected network of the ROIs, but one that was not significantly different in average total network connectivity.
Figure 7. Beat perception and maintenance (BPM) task contrast of strongly metrical – null stimuli. ($p<.05$)

Figure 8. Selected slices from Beat production and maintenance (BPM) task activation contrast of strongly metrical versus non-metrical stimuli. ($p<.05$)
between SM and NM trials in either. There were however statistically significant differences ($p<.05$) for a small grouping of particular ROI pairs dependent on task and beat strength. During BR task 1, connectivity decreased between the right anterior cerebellum and the left thalamus, SMA, and IPL for SM stimuli as compared to NM (Figure 10). The same was observed between the right IPL and SMA. In contrast, there was significantly increased connectivity ($p<0.05$) between the left PAC and bilateral putamen, and the right PAC with the left putamen. A similar, though non-significant trend was seen in the right putamen and corresponding PAC. During the production and maintenance task the left D/VLPFC showed significant connectivity increases with the bilateral PACs and SMAs for SM relative to NM stimuli (Figure 10). This same increased connectivity was found between the left thalamus and both D/VLPFCs, as well as between the right thalamus and left caudate.
Figure 10. Correlation Matrices for BR\textsubscript{(a)} and BPM\textsubscript{(b)} tasks. The upper right triangular region of each matrix is SM stimuli, lower left is NM stimuli. * = sig. stronger correlation coefficient ($p<.05$) than during comparison stimuli.
The network visualization of BR and BPM connectivity maps show present only the strongest network correlations \( r > .66, p < .01; \) (Figure 11). It demonstrates not only a greater number of strong connections overall for BPM as compared to BR, but a greater number of subcortical-cortical, intrastriatal, and intrahemispheric connections. More specifically, in both tasks it is apparent that the caudate nucleus and D/VLPFC of the left hemisphere seem to act as connectivity “hubs”. This does not seem to change with task behavior, but rather appears augmented, once production of a beat is required, via stronger internetwork coupling of the bilateral putamen, SMAs, parietal lobes and thalami. One can also see how the subcortical regions, SMAs, and D/VLPFCs strongly begin to synchronize when movement becomes necessary. It is important to note that while the BR task SM vs. NM correlation matrix showed significant differences in connectivity between the anterior cerebellum and a broad range of ROIs, as well as between the bilateral putamen and PACs, none of those connections would appear particularly robust relative to others in the network given their absence from Figure 10. In contrast, the BPM matrix showed left D/VLPFC connectivity significantly changed dependent on stimuli, and many of those same connections can be seen as being among the strongest in the network when producing SM stimuli (Figure 10). It is in this way that such a combination of visual representations provide a more nuanced picture of the whole, and will be important to future work in this area.
Figure 11. A graphical representation of those ROI pairings with the highest (>0.065) correlation coefficients for strongly metrical (SM) stimuli in either cognitive task. (p<0.01). Please note: Nodes do not correspond with exact anatomical location. This is a gross level approximation designed to give a general indication of cluster location. For example, basal ganglia were moved for ease of viewing.
CHAPTER 4

DISCUSSION

While the neurophysiological correlates of identifying and producing rhythm are relatively established, very little work has attempted to determine how these regions functionally interact. This study was therefore conceived as a multifaceted fMRI imaging approach to explore the differences between beat perception, production, and the connections underlying both these cognitive phenomena.

The behavioral tasks used to study rhythm perception appear to have been quite effective. Both the high performance rates in SM and NM conditions, as well as findings within all traditional ROIs, indicate the tasks elicited the desired behaviors and neural responses. Contrasts between SM and Null stimuli clearly showed higher BOLD signal in the bilateral PACs, SMAs and D/VLPFCs for both tasks. During BR there was also significant ($p<.01$) activation of the bilateral IPLs, caudate nuclei, putamen, thalami, and cerebellum. The BPM task elicited BOLD response ($p<.05$) in the left IFG. All these regions, as mentioned previously, are well established in the literature. Moreover the large overlap between regions activated during both production and perception is consistent with previous results by Chen, Penhune, et al. (2008a, 2008b), Chen, Zatorre, et al. (2006), and more recently Kung et al. (2013), indicating both behaviors recruit resources from the same network. The inverse activation shown in SM>Null/NullTap and NM>Null/NullTap contrasts (ie. Null>SM and Null>NM), we believe can largely be attributed to activity of the default mode network (DMN). It is likely that during the ~13 seconds of silence of Null trials, participant’s attention tended to wander and this is the root of these findings.

When comparing SM to the less rhythmic NM stimuli during BR and BPM, the strongest activation contrast occurred in the putamen. This closely resembles findings seen in work by Grahn and Brett (2007, 2009), Grahn and Rowe (2009) where activation in the putamen increased with beat strength. The additional activity found in the anterior ACC) and precuneus was unexpected as the papers by Grahn and colleagues report activation beyond the putamen in more common network areas (eg. cerebellum, STG, SMA, etc.) during both
volume and duration accented Beat vs. No Beat comparisons (similar to SM-NM). This divergence in findings is most likely due to differences in auditory stimuli; namely ours were both non-repeating and unaccented. Three sequential P&E patterns as compared to a singular repeating one during each trial could have required greater checking/error detection against internally predicted beat onsets. Given that both the ACC and precuneus are considered regions linked to self-awareness and interoception (Bush, Luu, & Posner, 2000; Lou et al., 2004), it seems likely the areas were activating in such a capacity. Why more traditional network areas, as those seen in Grahn’s study, were not similarly active remains uncertain.

When examining the difference in areas required for producing a beat as compared to rating it, more activation was found in the ACC which seems to lend credence to the error detection theory since production could quite conceivably require more internal comparisons than BR. That being said, any activation when comparing (SM > Null)$_{BR}$ vs. (SM > NullTap)$_{BPM}$ was unexpected given the Kung and colleagues (2013) finding that “[Find Beat vs. Listen Isochronous] versus [Tap Beat vs. Tap Isochronous]… revealed no regions that were significantly different in either condition,” (2013). The result however could be due to the two tasks having an unequal number of trials (ie. three BPM to six BR) and that in our protocol participants did not practice or learn rhythms before production. The additional activation we observed in the bilateral PACs, SMAs, and the putamen (Figure 9) could be due to greater resources being required to rapidly identify beat in novel rather than familiar stimuli.

Functional connectivity analyses showed, on average, network-wide connectivity is relatively stable regardless of stimuli or task. Differences in behavior would appear to stem from very specific, subtle changes in the synchronicity between particular regions. During the BR task there was significantly greater connectivity found between the bilateral putamen and the PACs. This finding resembles those from Grahn and Rowe (2009) where coupling between the putamen and the right STG rose as beat strength increased, with a similar trend in the left STG. However, we did not detect any stimulus-dependent increases in correlations between the putamen and the bilateral SMAs and PACs as they did. This can most likely be attributed to our use of more general time based correlations rather than their performance modulated PPI analyses which likely detect more subtle changes across conditions. During the BPM task there were significant increases in connectivity between the D/VLPFC and the
bilateral PACs and SMAs that occurred as participants tapped to SM as compared to NM stimuli. Interestingly this is somewhat in opposition of Kung and colleagues (2013) who found that right VLPFC “activity was more strongly coupled with activity in the right STG for the weak as compared with the strong metrical rhythms”. We are uncertain as to why this is the case. However, the study by Kung et al. employed experimental protocols similar to those in Chen et al., where stimuli were we presented and then repeated for tapping. It is therefore conceivable that these may have involved different cognitive processes. Tapping to a primed or learned beat may necessitate a decrease in D/VLPFC and STG connectivity to allow motor areas to functionally take over beat production; whereas novel tapping, where beat must be identified and generated simultaneously, could necessitate increased connectivity of these regions with motor areas. Our finding of increased signal synchronicity between the left D/VPLFC and not only the PACs but the bilateral SMAs would seem to support this view.

A final set of novel findings from this study is particularly important to note. Thus far, no FC study has examined the role of the thalamus within the beat network. Given its well-established anatomical pathways for auditory and motor processing, the thalami could plausibly be functioning in either capacity. However, our network map (Figure 10) indicates that connections between the left thalamus, and the bilateral caudate nuclei and SMAs are some of the strongest in the network during both BPM and BR. Follow up t-testing also revealed the bilateral thalami have significantly greater connectivity with the SMAs than with the PACs during both BR ($p=.002$) and BPM tasks ($p=.003$). Therefore we feel there is sufficient evidence to say the thalamus is primarily acting in a motor capacity during beat perception. Considering this information in congress with work done on the basal ganglia, the caudate and putamen in particular, in movement disorders like Parkinson’s and Huntington’s disease (Grahn & Brett, 2009), and in beat perception, we feel indicates a strong need for increased attention to the thalamus in clinical research. Its supportive role in motor function during a task with known deficits in those suffering from motor disorders seems to indicate the region has potential as a possible therapeutic intervention point.
LIMITATIONS & FUTURE DIRECTIONS

Although sample size in this study was comparable to many fMRI studies in healthy adults, power limitations may have prevented the detection of some true activation and connectivity effects. The exclusion of four participants' data due to movement artifacts and task response issues was a significant loss of data and indicates greater care should have been taken in pre-scan briefings and inter-scan direction reminders. Typically FC analyses utilize block design protocols for various reasons pertaining to later processing and analysis methodologies. Our dataset was not constructed with this type of analysis in mind, and as such our use of a rapid, interspersed, event-related design, rather than block, was not ideal for conducting these analyses. Future rhythm studies hoping to utilize FC techniques will benefit from a protocol designed specifically for such work.

Our use of correlation matrices as an analysis approach necessitated correlating each ROI against all others within the network, and hence beginning from the a priori assumption that all regions may connect to one another. This however does not take into account anatomical literature or indicate true neurophysiological connection in anyway. It is merely the nomenclature of the imaging field to describe correlations between regions as “connectivity.” These results cannot stand in place of more direct measures of neural connection such as diffusion tensor imaging (DTI) or electrophysiological studies. That being said, these correlation matrices and connectivity maps provide some of the first representations of the beat network as a whole.

It is also important to note that correlations by their nature are inherently non-directional and so our use of matrices and network maps are missing this very crucial piece of the puzzle so to speak. No work that we know of has attempted to use effective connectivity with rhythm behaviors. Our plan is that a subsequent analysis of these data with structural equation modeling methods will dramatically expand our understanding of this network, and help determine not only what regions are most likely interacting, but what is the probable direction of that signal between said regions.

CONCLUSION

This study replicated several findings from the literature. Namely, that both beat perception and production recruit neural resources from predominantly overlapping regions
of a single network. Also the basal ganglia, and in particular the putamen, are activated most strongly for metrical stimuli. Given our correlation matrices indicating connectivity increases between putamen and auditory cortical regions with increased beat strength, it seems possible this interaction may be vital for the putamen to perform their role in beat identification. Other results were unexpected and provided new hypotheses concerning the function of certain areas. The presence of significant BOLD response in the ACC and precuneus for instance raised questions concerning their potential role in error detection of internally produced rhythms. Finally, there were novel findings we feel provide important new investigative possibilities for clinical work. The evidence that thalami are acting principally as a supportive area to motor rather then auditory functions during beat perception indicates greater focus should be placed on the thalamus as a potential site for therapeutic intervention in individuals suffering from Parkinson’s and Huntington’s Diseases. Our data from both cognitive tasks show how strongly synchronized the thalami are with the basal ganglia, in particular the caudate; an area whose degeneration is shown to positively correlate with the neuropsychological deficits and dementia of Parkinson’s disease (Bruck et al., 2001; Rinne et al., 1989). We sincerely hope our subsequent effective connectivity work will not only help strengthen the scientific community’s conceptual grasp of the rhythm network, but also contribute further information towards clinical work and therapeutic applications.
REFERENCES


Table 1. Listing of Regions of Interest (ROIs) Utilized for Within Network Analyses. Clusters Determined via Use of Variable Thresh-Holding of Task 1 (SM > Null) Activation Contrast, and “Cluster to Whole-Brain” Analyses

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Voxel Count</th>
<th>Center of Mass (Talairach Coordinates x y z)</th>
<th>Brodmann’s Area(s) If applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>L Superior Temporal (Primary Auditory Cortex - PAC)</td>
<td>28</td>
<td>+44.3 +19.0 +8.3</td>
<td>41 22 13</td>
</tr>
<tr>
<td>L Dorsal/Ventrolateral Prefrontal Cortex (D/VLPFC) (+ Insula)</td>
<td>28</td>
<td>+46.3 -7.9 +16.3</td>
<td>44 9 13</td>
</tr>
<tr>
<td>L Supplementary Motor Area (SMA) (+ supramarginal gyrus)</td>
<td>24</td>
<td>+4.2 +8.5 +53.8</td>
<td>6</td>
</tr>
<tr>
<td>L Inferior Parietal Lobule (IPL)</td>
<td>28</td>
<td>+41.6 +39.1 +38.1</td>
<td>40</td>
</tr>
<tr>
<td>L Posterior Lobe of Cerebellum (+culmen)</td>
<td>28</td>
<td>+22.1 +53.6 -45.6</td>
<td>Lobule VIII</td>
</tr>
<tr>
<td>L Anterior Lobe of Cerebellum (+culmen)</td>
<td>24</td>
<td>+27.0 +52.2 -22.8</td>
<td>Lobule VI</td>
</tr>
<tr>
<td>L Putamen</td>
<td>12</td>
<td>+21.0 -0.3 +7.3</td>
<td>-</td>
</tr>
<tr>
<td>L Caudate Nucleus</td>
<td>15</td>
<td>+14.8 -1.7 +14.7</td>
<td>-</td>
</tr>
<tr>
<td>L Thalamus</td>
<td>17</td>
<td>+11.4 +14.6 +10.1</td>
<td>-</td>
</tr>
<tr>
<td>R Superior Temporal (Primary Auditory Cortex - PAC)</td>
<td>28</td>
<td>54.6 +20.4 +7.6</td>
<td>41 22 21</td>
</tr>
<tr>
<td>R Dorsal/Ventrolateral Prefrontal Cortex (D/VLPFC) (+ Insula)</td>
<td>23</td>
<td>-52.4 -9.3 +20.3</td>
<td>44 45 9</td>
</tr>
<tr>
<td>R Supplementary Motor Area (SMA) (+ supramarginal gyrus)</td>
<td>26</td>
<td>-6.0 -1.8 +50.6</td>
<td>6 32 24</td>
</tr>
<tr>
<td>R Inferior Parietal Lobule (IPL)</td>
<td>27</td>
<td>-45.7 +40.4 +39.4</td>
<td>40</td>
</tr>
<tr>
<td>R Posterior Lobe of Cerebellum (+culmen)</td>
<td>24</td>
<td>-21.5 +54.3 -44.3</td>
<td>Lobule VIII</td>
</tr>
<tr>
<td>R Anterior Lobe of Cerebellum (+culmen)</td>
<td>23</td>
<td>-17.8 +48.0 -16.9</td>
<td>Lobules VI + V</td>
</tr>
<tr>
<td>R Putamen</td>
<td>14</td>
<td>-22.9 -3.3 +4.6</td>
<td>-</td>
</tr>
<tr>
<td>R Caudate Nucleus</td>
<td>13</td>
<td>-13.4 -5.5 +13.5</td>
<td>-</td>
</tr>
<tr>
<td>R Thalamus</td>
<td>14</td>
<td>-13.1 +13.9 +10.9</td>
<td>-</td>
</tr>
</tbody>
</table>