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The overarching purpose of the present study was to investigate the effects of music listening experiences on the human brain through the application of network science methods. To this end, several questions were explored. First, what are the effects of listening to different music genres on functional brain connectivity? Second, what are the effects of listening to preferred music—regardless of genre—on functional connectivity? Third, what are the effects of listening to a personally favorite song on the functioning brain?

Twenty-one participants listened to six randomly presented musical selections (i.e., hereafter, referred to as songs) in an uninterrupted manner while undergoing functional magnetic resonance imaging (fMRI) with their eyes closed at rest. The songs included four iconic songs from: rock, rap/hip hop, country, and classical genres. Additionally, there was an unfamiliar (i.e., Chinese Opera) and a personally favorite song that was self-reported during the screening session. Participants rated their preference following each song using a visual analog scale (VAS). The fMRI data were grouped for comparison by condition based on genres and participants' most preferred and least preferred song based on their highest and lowest VAS scores. The data collected, while participants listened to their favorite song, were analyzed separately. To clarify further, preferred music can be conceptualized as music listening experiences through public or online preferential music listening platforms, such as the radio, Pandora or Grooveshark. On the other hand, a personal favorite song may not be categorized specifically within the same genre as an individual's preferred music listening preference. Network science techniques were applied to the fMRI data to evaluate brain connectivity differences based on the conditions (i.e., genres, most preferred, least preferred, and favorite song). Results revealed that listening to classical music affects the degree of connectivity within the auditory cortex of the brain differently from other genres. Based on participants' highest and lowest VAS score, results also revealed that listening to music that is preferred, regardless of the genre, connects patterns of functional connectivity within a circuit important for internally-focused thoughts known as the default mode network. This network has been implicated in facilitating important brain functions such as the capacity to experience self-related thoughts and the ability to image the future and reflect on the past (i.e., mind-wandering or day-dreaming). Finally, listening to a self-reported favorite song revealed functional changes in brain connectivity between the auditory cortex and the hippocampus, a region responsible for memory encoding and social-emotion consolidation. These results suggest that network science offers a promising new method to study the effects of music on the brain. The neurorehabilitation, neurobiological, and educational implications of music listening are discussed.

NETWORK SCIENCE AND THE EFFECTS OF MUSIC ON THE HUMAN BRAIN

by

Robin W. Wilkins

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Intuitively, as human beings, we understand the power of music. It moves us emotionally, when words alone are insufficient. This manuscript is dedicated to the teachers and performers of music and the scientists who endeavor to study musical phenomena. May we soon discover the power behind our craft, when we examine the effects of music on the human brain.

APPROVAL PAGE

This dissertation written by ROBIN W. WILKINS has been approved by the following committee of the Faculty of the Graduate School at the University of North Carolina at Greensboro.

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It is a not a cliché to say that no one achieves anything without help. This is particularly true when conducting interdisciplinary research. Exceptional thanks go to my advisor, Dr. Donald Hodges, for his expertise and continual support of my intent to pursue experimental neuroscience research with music. Equally important, a special thank you for his willingness to expedite my research efforts by introducing me to Dr. Paul Laurienti, Director of the Laboratory for Complex Brain Networks (LCBN) at Wake Forest University Baptist Medical Center and Dr. Jonathan Burdette, neuroradiologist for the LCBN. Working at the LCBN for three years was exactly what I needed to pursue my goals. Their combine efforts enabled me to apprentice in the lab, conduct my research, receive expert brain imaging and network science technical training, and present and publish my research. By his helping me renegotiate my doctoral program and assistantship to include brain imaging and apprenticeship training at Wake Forest, I have been able to pursue my goal of becoming a neuroimaging scientist.

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LIST OF ABBREVIATIONS

BOLD:	Blood-oxygen level dependent
CBF:	Cerebral Blood Flow
CSF:	Cerebrospinal Fluid
DMN:	Default mode network
EEG:	Electroencephalography
EGLOB:	Global Efficiency
ELOC:	Local Efficiency
EPI:	Echo-planar imaging
fMRI:	Functional Magnetic Resonance Imaging
FSL:	Free Software Library
HRF:	Hemodynamic Response Function
ELOC:	Local Efficiency
MEG:	Magnetoencephalography
MNI:	Montreal Neurological Institute
PET:	Positron Emission Tomography
ROI:	Region of Interest
SPM:	Statistical Parametric Mapping
TE:	Echo time
TR:	Repetition time

CHAPTER I

INTRODUCTION

Background of the Problem

Perhaps more than any other external stimuli, music remains one of the most mysterious and least understood perceptual experiences of the human mind (Ball, 2008). From the time of ancient Greek philosophers, such as Aristotle to contemporary thinkers, fundamental questions about music continue to intrigue, engage, and confound both philosophical and scientific communities. These basic questions include the following. Why does music exist? Where did music come from? How does the mind 'understand' music? (i.e., perceive music as being meaningful), and why, throughout time and across cultures, do people enjoy and spend so much time with music? (Merker, Madison, & Eckerdal, 2009; Mithen, 2006; Panksepp & Bernatzky, 2002). To the lay listener, the connection between music and the human emotional response system seems obvious, and there has never been a culture without music; indeed, music is such a part of human life that music is implicated in how we define ourselves as human beings (Kivy, 2002). Thus far, scientific evidence to support any particular notion as to why is lacking considerably (Fitch, 2006). Speculation and theories abound, but these basic scientific questions remain (Cross, 2003; Jackendoff & Lerdahl, 2006; Mithen, 2006; Perlovsky, 2010; Sloboda, 2008). Nervertheless, people consider music to be one of their most meaningful and, curiously enough, regularly experienced aspects of their daily lives

(Hodges & Sebald, 2011). Biological researchers suggest that if music serves no specific evolutionary purpose for any particular human benefit, it should arguably have been extinguished long ago (Peretz, 2006; Peretz & Hebert, 2000). On the contrary, the human experience with music persists (Hodges & Sebald, 2011; Sacks, 2006). Mounting evidence indicates that there exists a host of potential neurological and cognitive benefits from experiences with music and formal musical training (Schlaug, Forgeard, Zhu, Norton, & Winner, 2009; Schlaug, Norton, Overy, & Winner, 2005). These benefits include human growth and development and educational and clinical health benefits (Kraus et al., 2014); Schlaug, 2009; Schulze & Koelsch, 2012). Indeed, with advancements in technology, music is more ubiquitous and freely available than ever before (Hodges & Sebald, 2011). Why does music, a seemingly non-imperative set of fleeting sounds, remain a common characteristic found across global human life? Regardless of the musical activity, there is, fundamentally—at the core of every individual's experience—some form of interaction. This ubiquitous human experience occurs in the brain.

Music connects a vast and diverse set of intricate neural processing networks (S. Brown, Martinez, Hodges, Fox, & Parsons, 2004; Peretz & Zatorre, 2005; Zatorre & McGill, 2005; Zatorre, 2003). These networks include structural components associated with sensory-motor processing as well as functional elements implicated in memory, cognition, and mood or emotional fluctuation (S. Brown, Martinez, & Parsons, 2004; Janata, 2005). Musical experiences influence human behaviors, speech and language processing, brain plasticity, spatial reasoning, the mirror-neuron system, and a host of clinical health recoveries (Soto et al., 2009).

Often connecting powerful emotions to memories, music is linked to outstanding questions surrounding levels of human awareness (i.e., the subjective experience), the emergence of consciousness, and theory of mind—the ability to understand the intentions and emotions of others (Damasio, 1994, 1999; Molnar-Szakacs & Heaton, 2012; Perlovsky, 2010; Tononi & Koch, 2008; Werner, 2009).

Though still a scientific frontier, present-day researchers are making substantial strides to advance our scientific understanding of the effects of music on the human brain (Janata, 2009; Koelsch, 2009; Perani et al., 2010; Peretz & Hebert, 2000; Trehub, 2003). Emerging evidence hints at powerful health, developmental, and evolutionary contributions from music (Koelsch, Schroger, & Gunter, 2002; Perlovsky, 2012; Salimpoor, Benovoy, Larcher, Dagher, & Zatorre, 2011; Schlaug, Marchina, & Wan, 2011). Yet, while glimpses of insight have surfaced regarding how music influences brain function, many fundamental questions remain. Research on the benefits and effects of the music as a phenomenon for understanding and remediating the brain remain considerably underexplored (Ball, 2008; Zatorre & McGill, 2005).

One of the most challenging neuroscientific questions is how listening to music connects brain systems associated with emotional processing and memory (Damasio, 1999; Gabrielsson & Bradbury, 2011; Juslin & Sloboda, 2001). People primarily choose to listen to music that they prefer or ‘like’ (Bharucha, Curtis, & Paroo, 2006). When listening to strongly preferred music, people report they frequently experience deeply personal, often emotionally-laden, thoughts and memories. Listeners describe that such impromptu self-referential thoughts and memories can be triggered spontaneously by different types of music and by the presence or absence of lyrics (Altenmüller, Schurmann, Lim, & Parlitz, 2002; Gabrielsson & Bradbury, 2011; Juslin & Vastfjall, 2008). Musical preferences, however, are highly individualized (Juslin & Vastfjall, 2008; Rentfrow & Gosling, 2003), and different types of music genres vary greatly in their lyrics and melodic, harmonic and rhythmic complexity (Wilkins, Hodges, Laurienti, Steen, & Burdette, 2012). To date, how listening to different kinds of music can generate mental experiences of similar types in different people remains unclear (Gabrielsson & Bradbury, 2011; Juslin & Sloboda, 2001). Unlocking these similarly experienced brain mechanisms in different people may provide insight into how the brain's mental architectural system associated with personal identity and individualized self-awareness is constructed as 'an individual mind'. A fuller understanding of how the brain achieves mental individuality, as scaffolding generated from uniquely personal thoughts and memories about personal experiences—all components of self-identity and self-awareness—might be possible.

Although the questions surrounding music and the mind are compelling, studying how the brain is affected by music—as people actually experience it—is challenging. Brain imaging techniques, such as functional magnetic resonance imaging (fMRI), have been focused on capturing snapshots of the brain that are necessarily time constrained for adequate scientific analysis. Researchers pursuing traditional brain imaging studies with music have analyzed brain responses to the pitches of single notes, a few chords, or brief multi-second excerpts (Brattico et al 2011; Blood and Zatorre, 2001; Blood Zatorre, Bermudez and Evans, 1999; Janata, 2009). Listening to music, however, is more than a single or multi-second event. When people listen to music, their individual responses to the experience evolve, often manifesting as a myriad of conflated mental and emotional responses, over the course of time. The experience appears to knit together a host of intricate mental states within the brain that are tagged emotionally. Neuroimaging studies must account for these aspects for the experience to be understood. If neuroimaging studies could account fully for these dynamic responses, perhaps new valuable information might be uncovered.

Traditional neuroscientific methods using functional magnetic resonance imaging (*fMRI*)[1] have focused on understanding brain function by locating discrete regions or 'areas' that are functionally related to particular tasks. A traditional neuroimaging approach is designed to determine how a few *voxels,* as tiny pixels of tissue, essentially 'light-up' within the brain during a specific task. Using fMRI to determine which isolated *voxel(s)* contributes to which underlying functional element within a specific task, therefore, has been limited, particularly for fMRI music research. Listening to music appears to activate and connect regions throughout the entire brain (S. Brown, Martinez, & Parsons, 2004). Studying single activation sites that respond to any particular characteristic within a musical composition (e.g., pitch, duration or timbre) has limited the scope of neuroscientific music research. For example, to measure how music affects

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[1] All words marked in italics are defined in the Glossary located at the end of the document.

brain-site activation, traditional neuroimaging studies often have been limited to using single tones, a few chords, or brief excerpts (Blood & Zatorre, 2001; Blood, Zatorre, Bermudez, & Evans, 1999; Koelsch, 2005). However, human responses to music are complex and dynamic. Responses to music are automatic but often include a host of mental states that can change rapidly across time. Listening to music can conjure up mental responses involved in thoughts, memories, mood changes and emotions. Listening to music may affect physical movements and body regulation, such as foot tapping, hand clapping, marching, and dance. Measuring how the brain responds to a single chord or brief excerpt ignores vast amounts of neuroscientific information.

Further constraining neuroimaging research, the brain is not static (Buzsaki & Draguhn, 2004; Raichle, 2010). The brain is constantly in flux and ‘re-wiring’ itself, based on demand. Trying to understand brain function by measuring single activation sites is like trying to transcribe a symphony by hearing two or three notes. Auditory stimuli, such as music, are processed within milliseconds. Techniques, such as fMRI, can measure signals of activity from structures deep within the brain at a relatively high spatial resolution (3x3x3mm), but require several seconds to capture the signaling response. *Electroencephalography* (EEG), another useful technique in brain imaging, can measure temporal signal activity on the surface of the brain within milliseconds, but does not allow for the deep spatial resolution of fMRI. A new approach has been needed to more fully understand the dynamic changes in the human brain and account for the cognitive, emotional and perceptual sensory-motor responses to the phenomena of music.

Network Science: A New Approach

Network Science is a rapidly emerging field for studying complex systems in terms of their components and the interactions among these components (Barabasi & Albert, 1999). Based on graph theory, network science methods are statistical techniques designed to capture and measure specific characteristics of a network as an interconnected system (Watts & Strogatz, 1998). There is perhaps no more complex system than the human brain. Network science methods measure complex systems in terms of their components and the interactions among them (Sporns, Chialvo, Kaiser, & Hilgetag, 2004). Embracing the brain as a complex system offers the opportunity to uncover patterns of inter-regional brain connectivity and generate an increased understanding of how structural connectivity contributes to dynamic brain function (Bassett & Bullmore, 2006; Bullmore & Sporns, 2009; Rubinov & Sporns, 2010). In application, a network-based approach to the brain is different from more traditional neuroimaging approaches. Rather than measure a single activation site in comparison to a stimulus, network science techniques measure whole-brain responses to a stimulus by comparing each brain activation site to each and every other activation site throughout the brain network.

Network science provides a host of statistical techniques to measure both structural and functional connectivity throughout the entire brain, as is described subsequently. This methodology can capture how the brain network changes during different brain states and psychiatric or neurological disorders. A network science approach offers a substantial advance in neuroscience and an unprecedented opportunity for music neuroimaging research. Because listening to music affects such intricate and diverse brain systems, a response to music is an ideal candidate for network analysis. Several research questions, therefore, were formulated for the present series of exploratory studies, as highlighted in the following section.

Purpose of the Series of Studies

The present series of exploratory studies was designed to investigate the effects of music on the brain through the application of network science methods. The purpose of each study within the series was to apply network science techniques to brain imaging data acquired during functional magnetic resonance imaging (fMRI) while people listened to complete songs from a variety of musical genres.

Based on the outstanding questions within neuroscience related to music listening, and the related literature available, several questions were formulated for the present set of investigations.

1. Does listening to different genres of music, such as rap, rock, country or classical music, change brain network connectivity?
2. Does music listening preference, regardless of genre, change functional brain connectivity? If so, do changes occur within the posterior medial cortex regions of the brain responsible for the support of introspective thought, emotion reprocessing, and rumination of personal memories (i.e., the default mode network)?
3. Does listening to a self-reported favorite song, regardless of the genre in the presence or absence of lyrics, change functional brain connectivity? If so,

does listening to a favorite song change functional connectivity within the regions responsible for the encoding of emotionally-laden memories?

This dissertation evolved from a series of exploratory network science brain imaging studies using real-world music listening. Network science methods account for changes throughout the network of the brain. As an emerging field, however, future development of new network techniques, including their application to multimodal neuroimaging, will be helpful to address rapid temporal changes within the brain network that may occur when listening to music.

CHAPTER II

REVIEW OF THE LITERATURE

To understand the experiments in this manuscript, a broad overview of major themes is provided in Chapter II. These themes include: (a) Network Science, (b) A Network Science Approach to the Brain, and (c) The Default Mode Network. Additional other topics are reviewed, including: (a) Music and the Brain, (b) Emotional Responses to Music and (c) Music Preferences. Detailed discussions about these themes and topics are contained in Chapters III and IV and are included in the Appendices.

Network Science: The Study of Complex Systems

Network Science is a rapidly emerging field for studying complex system in terms of their components and the interactions among these components (Strogatz, 2001; Watts & Strogatz, 1998). Steeped in the mathematical foundation of graph theory, network science techniques can be used to quantify elements of a complex system as components and can be used to measure the relationships among these components (Boccaletti & Pecora, 2006; Newman, 2003; Strogatz, 2001). There are numerous examples of complex systems from the physical, biological and social sciences that can be represented as networks. For example, there is the Internet—computers linked by data connections—and Facebook, a human network connected by behaviors or social interactions. Indeed, many examples of networks exist in the world. There are structural networks, such as roads that connect cities and towns, ecosystems, the World Wide Web, and the wide variety of human social networks (Strogatz, 2001). The discovery of network properties, as unique characteristics, can provide useful information about how a specific network is structured and how it functions as a complex system (i.e., a cohesive whole). This information could include how a computer works based on its individual parts, how a national economy functions, or how humans interact on social networking platforms such as Facebook or LinkedIn. Importantly, the patterns of connections—as measurements of ongoing active connectivity— are crucial to understanding how a complex system functions. Drawing from the mathematical, computational, and statistical sciences, network science techniques provide robust tools to analyze, model and study patterns within networks (Newman, 2003). These patterns provide meaningful insight into the network as an interconnected, complex system.

Graph Theory: The Underpinnings of Network Science

Network Science is a field of study based on a branch of mathematics called graph theory (Newman, 2003). A graph is a mathematical representation of any real-world network that is made up of interconnected elements. In its most basic form, a network is simply a collection of points, referred to as vertices or nodes connected by lines as links or edges (see Figure 1). A simple graph is a set of nodes that has a set of edges. Nodes represent the fundamental elements of the system, such as people, and the edges represent the connections between pairs of nodes, such as the friendships between pairs of people. Thus, a network is defined as a set of *nodes* or vertices and the connections between them as links or edges. For a complete review of the network theory see Newman (2010).

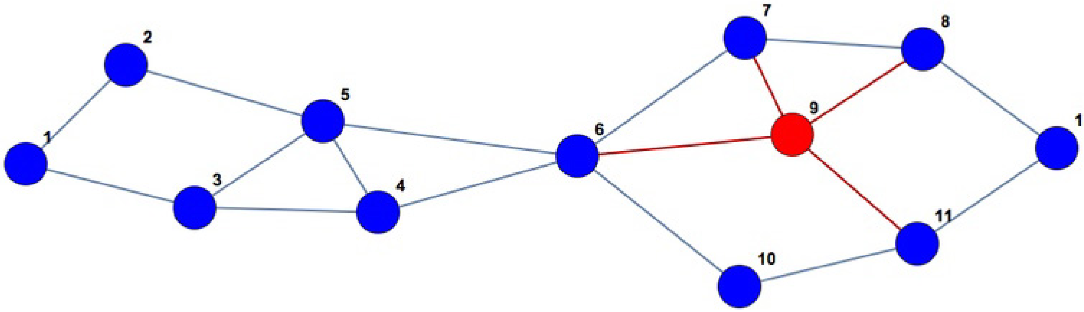


Figure 1. Simple Network. Demonstration of a network. This simple network is comprised of 13 nodes. Nodes are vertices (shown in blue). Nodes are connected to other nodes by edges as links (shown in red).

Within a network, the degree of a node is simply the number of connections the node has to other nodes within the network (Strogatz, 2001). Degree is most often denoted with the letter *K* (see Figure 2) (Bullmore & Sporns, 2009). The degrees of all the nodes within the network form a *degree distribution* (Amaral, Scala, Barthelemy, & Stanley, 2000). In random networks, where all connections are equally possible, the degree distribution result is typically Gaussian (i.e., normal) with a symmetrically-centered distribution. Complex networks, on the other hand, generally result in a non-Gaussian degree distribution with a long tail toward high degree nodes. The degree distribution of complex networks typically follows a power-law resulting from the preferential attachment of high-degree nodes connecting to other high-degree nodes and is thus scale-free (Barabasi & Albert, 1999). A scale-free network is one that contains certain high-degree nodes that preferentially attach to other high-degree nodes that far surpass the average. These high-degree nodes are referred to as ‘hubs’. Due to the presence of hubs, a scale-free network strongly correlates with the network's robustness in avoiding failure.

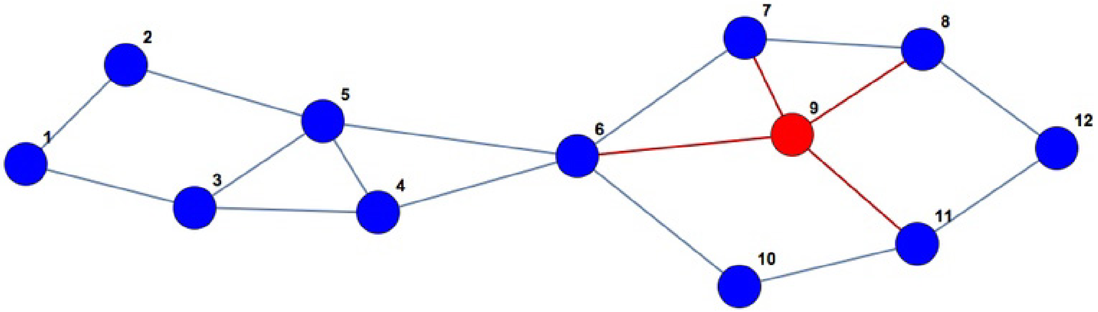


Figure 2. Demonstration of Node Degree (K). This network depicts that node 9 (shown in red) is connected by edges or links to four other nodes in the network. Thus, it would have a Degree (K) of 4. In contrast, Node 6 has a degree of 5.

In the depiction of the network shown in Figure 2, blue nodes are connected by links (shown in gray). Node 9 (shown in red) has edges or links that connect it to four other nodes within the network. Thus, the node has a degree (*K*) of 4. Node 6, on the other hand, connects to five other nodes in the network; node 6 has a degree (*K*) of 5.

The number of connection links, or pathlength, is calculated by measuring the minimum number of edges each node signal must pass through while en route to its final destination within the network. This measurement can be compared to a network with the same number of nodes and the probability of a randomly generated set of connection links within the same network. Thus, in any collection of nodes within a network, the degree of the collection can be compared to the degree that might occur in a randomly connected network of the same size or density (i.e., total number of nodes within the network).

In the Figure below, we can see that all the nodes within the network have the equal probability of connecting to each and every other node within the network (see Figure 3). If all the nodes connect to all the other nodes, we would say that the network is regular (i.e., completely connected). If, on the other hand, we investigated the possibility of the connections of a node within a random network, we would see a different result. In random networks, all degree connections are equally probable, resulting as a Gaussian degree distribution.

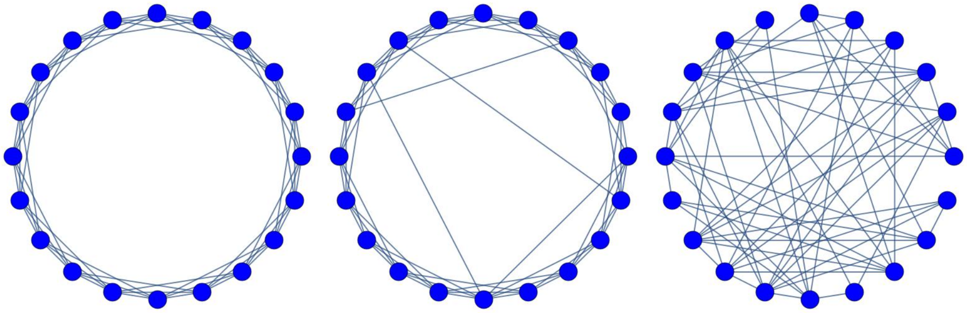


Figure 3. Depiction of Three Networks: Regular, Small World and Random. In the regular network, (shown on the left) all nodes are connected to each other. The regular network is completely connected. In the random network, (shown on the right) all connections are arbitrary. The middle network depicts how most nodes are connected to nearby neighboring nodes, but a few nodes have direct long-range connections. The result is termed the small world network.

In a regular network each node is connected to its nearest neighbor and its neighbor's nearest neighbor (see Figure 3). In this case, the regular network is considered completely connected. However, in the random network, not every node is connected to its nearest neighbor (Figure 3). The node connections are within the network, but not every node is connected to its nearest neighbors. The connections are more arbitrary and the network is comprised of randomly selected connections. In contrast to both the regular and the random network in Figure 3, the network shown in the middle reveals that most nodes connect to neighboring nodes, but a few nodes have long-range connections to other nodes in the network. Thus, while the network has many node-to-nearest-neighbor connections, it also has a few distinct long-range connections. From a practical sense, this figure illustrates that having direct connections, without a node signal having to go through it's nearest neighbors, means that certain nodes in the network appear to have an advantage. These nodes do not have to communicate their signal through connections to other nodes in the network to reach a specific node destination. These nodes experience direct communication connectivity to nodes that are not their nearest neighbors. These non-neighbor direct connections are found regardless of node location (i.e., regional proximity). This phenomenon is referred to as a '*small world network*' and is a characteristic of complex brain networks (Bassett & Bullmore, 2006; Watts & Strogatz, 1998).

In random networks, all node degree connections are possible. In most complex systems however, high degree nodes tend to connect to other high degree nodes. The brain operates in a similar manner. Intuitively, when considered as a framework application to the brain, this pattern makes sense. The brain selectively utilizes its high degree connections as primary resources in an efficient fashion to facilitate and coordinate a host of widely distributed system-level functions.

To recap, nodes in complex networks, such as the brain, generally have a non-Gaussian degree distribution often with a long tail towards a high degree. Complex systems exhibit characteristics of small-world networks where nodes tend to connect to other nodes in disparate regions of the network. Finally, exceedingly high degree nodes tend to attach to other high degree nodes preferentially and, thus, the degree distributions in complex networks typically follow a power law (Barabasi & Albert, 1999).

If the nearest neighbors of a node are also directly connected to each other they form a cluster (Watts & Strogatz, 1998). Nodes that tend to cluster are considered *hubs*. As the term implies, hubs function as major areas of communication within the network. The *clustering coefficient* quantifies the number of connections that exist between the nearest neighbors of a node as a proportion of the maximum number of possible connections. Random networks have a low average clustering whereas complex networks typically have high clustering. This phenomenon is important when considering application to the brain. Nodes with high degrees, as hubs, are considered important because they are central to the network (see Figure 4).

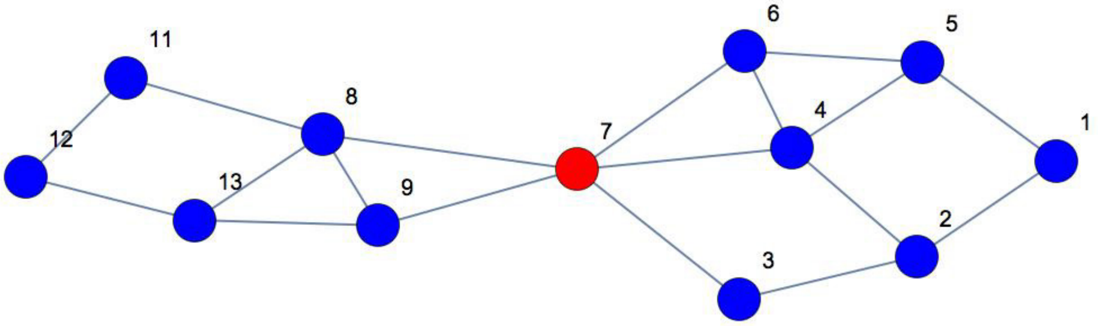


Figure 4. Demonstration of a Hub. Node 7, shown in red, is central to all the other nodes in the network and is a hub. Note that node 7 has a degree (K) of 5, and is considered a hub within the network due to its high centrality.

Hubs are part of a class of network measurements termed *centrality.* Centrality measures how many of the shortest paths between pairs of nodes a node signal must pass through on its way to its final destination within the network (See Figure 4). There are several approaches to calculate characteristics of brain centrality (Joyce, Laurienti, Burdette, & Hayasaka, 2010). Somewhat like major interchanges on an interstate highway or subway station transfer-stops, central nodes as hubs play an important role in the network. A node with high centrality, as a hub, is considered crucial to the network. As one could envision in Figure 4, if the hub is damaged or removed, the network will become fragmented and signal communication across the network will be affected accordingly.

Evidence reveals that sustaining a network requires the maintenance of specific hubs that have high degree connections as node clusters that may be located in unique or hidden regions (Bullmore & Sporns, 2009). The selection and removal of a few critical nodes as hubs can wreak havoc and dismantle the entire network (Albert, Jeong, & Barabasi, 2000). Again, this has implications for the brain. Regional damage or trauma to specific hubs would likely have impact on the brain functional network.

Assortativity is the correlation between the degrees of connected nodes. Positive assortativity means that high degree nodes tend to self-select to other high degree nodes. These degree distributions, where high degree nodes connect to other high degree nodes, result in the small-world phenomenon (Barabasi & Albert, 1999; Watts & Strogatz, 1998). A negatively assortative network, on the other hand, indicates that high degree nodes tend to connect to low degree nodes.

Community structure is a sub-global measurement of the interconnectedness of nodes within a network (Newman & Girvan, 2004). Similar in concept to subsets or neighborhoods, community structure measures the topological configuration of the network (see Figure 5) by calculating nodes that share more inner connections than outer connections, thus creating non-overlapping groups or communities of nodes within the network (see Figure 6). In community structure, the network is subdivided into modules. Modules are specific arrangements of nodes in the network that share more interconnections than outer connections (Bullmore and Sporns, 2012). A more precise description is that community structure indicates the maximum number of within-group edges and minimizes the number of between-group edges (see Figure 7). A community structure matrix can also be generated to depict which network nodes connect more to each other, as modules, than to other connecting nodes (see Figure 8). In Figure 8, nodes sharing inner connections are shown as purple. Note that modules are not spatially dependent. In other words, communities or modules of nodes can reside in distant locations within the network, yet still share inner connectivity. In essence, communities are topological subsystems of subsystems within a network. Another term for community structure within a network (i.e., nodes that share connections with each other as non-overlapping groups) is *modularity.*

In summary, this section highlighted the fundamentals of graph theory and network science. In any network, there can be different —yet potentially equally informative— measurements about the components of a network. Network science techniques account for characteristics of the network by measuring specific components and their unique interactions (Telesford, Simpson, Burdette, Hayasaka, & Laurienti, 2011). Each layer or piece of information leads to a fuller understanding of the network by providing different, yet complementary, information about how the network functions as a system. For a complete review of network measurements see Rubinov and Sporns (2010).

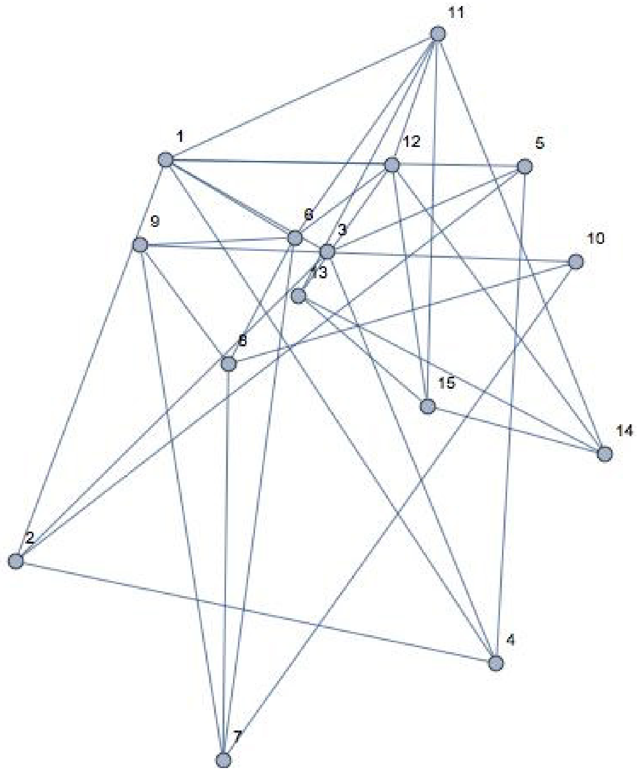


Figure 5. Depiction of a Network. This figure demonstrates node connections within a network but does not indicate community structure.

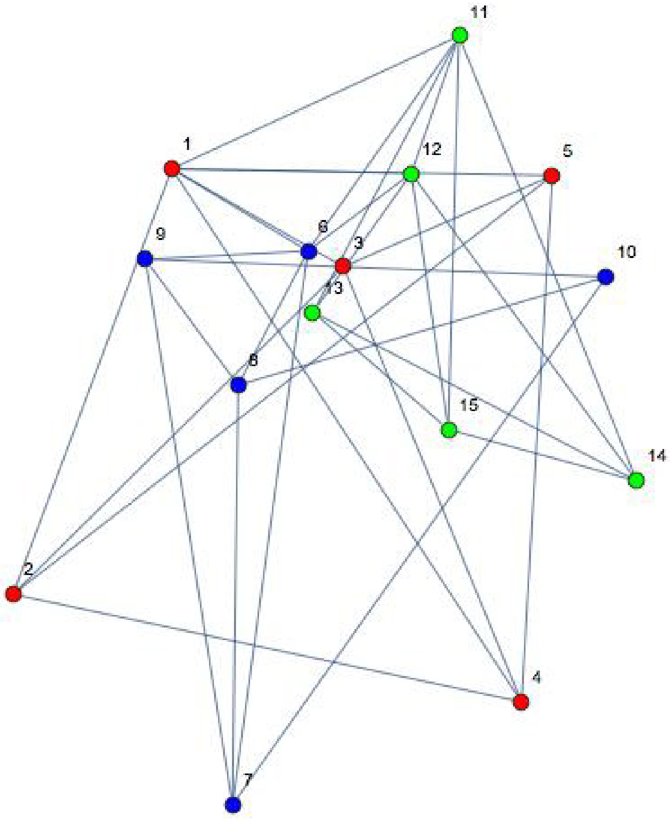


Figure 6. Demonstration of Node Connections. This figure depicts how nodes can exhibit more inner connections as modules (shown by color) than outer connections within a network.

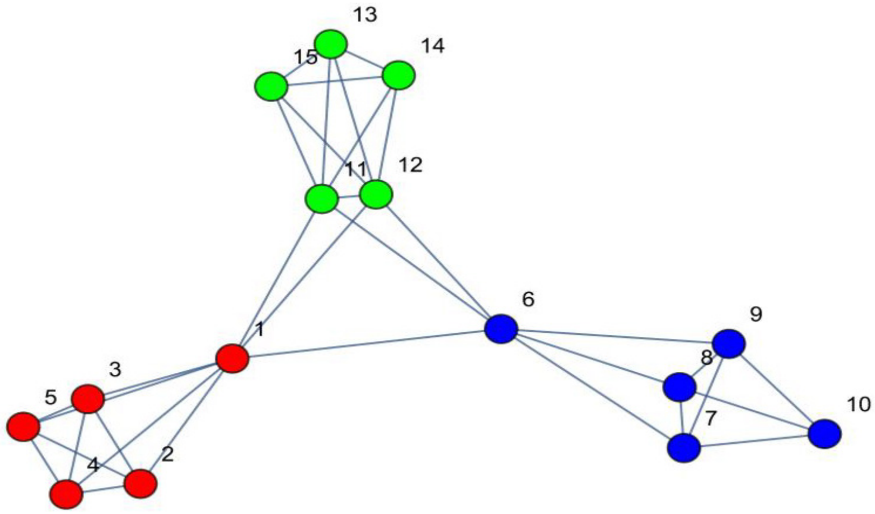
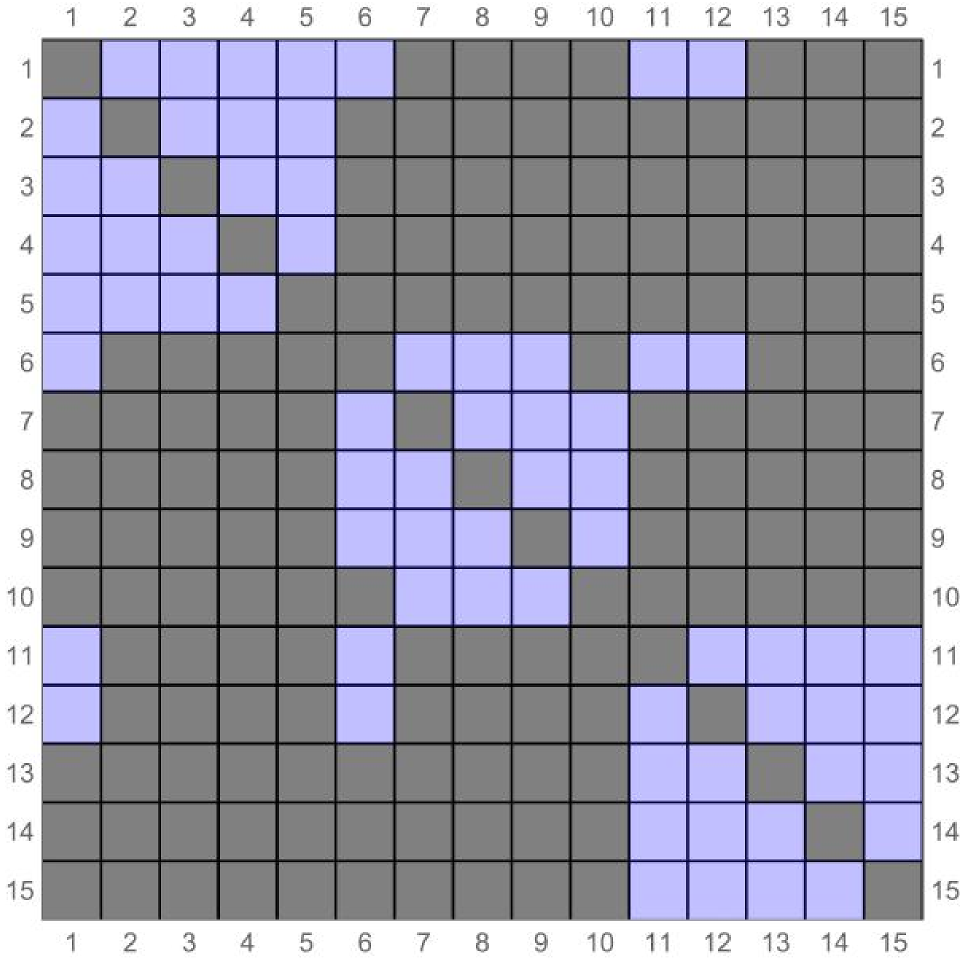


Figure 7. Demonstration of Node Communities. This figure depicts node communities (or modules) within the overall network. Nodes that share more inner connections to each other than to other nodes in the network form a module. Modules, as communities, can exist despite node location or proximity.



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	⬛	🟪	🟪	🟪	🟪	🟪	⬛	⬛	⬛	⬛	🟪	🟪	⬛	⬛	⬛
2	🟪	⬛	🟪	🟪	🟪	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛
3	🟪	🟪	⬛	🟪	🟪	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛
4	🟪	🟪	🟪	⬛	🟪	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛
5	🟪	🟪	🟪	🟪	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛
6	🟪	⬛	⬛	⬛	⬛	⬛	🟪	🟪	🟪	⬛	🟪	🟪	⬛	⬛	⬛
7	⬛	⬛	⬛	⬛	⬛	🟪	⬛	🟪	🟪	🟪	⬛	⬛	⬛	⬛	⬛
8	⬛	⬛	⬛	⬛	⬛	🟪	🟪	⬛	🟪	🟪	⬛	⬛	⬛	⬛	⬛
9	⬛	⬛	⬛	⬛	⬛	🟪	🟪	🟪	⬛	🟪	⬛	⬛	⬛	⬛	⬛
10	⬛	⬛	⬛	⬛	⬛	⬛	🟪	🟪	🟪	⬛	⬛	⬛	⬛	⬛	⬛
11	🟪	⬛	⬛	⬛	⬛	🟪	⬛	⬛	⬛	⬛	⬛	🟪	🟪	🟪	🟪
12	🟪	⬛	⬛	⬛	⬛	🟪	⬛	⬛	⬛	⬛	🟪	⬛	🟪	🟪	🟪
13	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	🟪	🟪	⬛	🟪	🟪
14	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	🟪	🟪	🟪	⬛	🟪
15	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	⬛	🟪	🟪	🟪	🟪	⬛

Figure 8. Demonstration of Community Structure in Matrix Format. Community Structure can also be represented in a matrix format. In this figure, an inner connection is shown in purple. An absence of an inner connection is shown in gray.

A Network Science Approach to the Brain

In terms of application to the brain, a network-based neuroscientific approach is different from a traditional neuroscientific approach (Sporns et al., 2004). Using a more traditional approach, scientists typically set out to determine which tiny areas, as isolated sites within the brain, activate during a stimulus. In contrast, a network approach does not seek to measure single activation sites. Rather, scientists measure activity patterns of brain connections throughout the whole brain (Bullmore & Sporns, 2009). Depending on the investigation, evidence of unique patterns of connections can reveal how a stimulus, a mental condition or damage affects the entire brain (Bassett & Bullmore, 2009). Thus, by measuring activity patterns of connectivity across the entire brain, network techniques provide a powerful new way to represent both the brain's structural and functional systems (Achard, Salvador, Whitcher, Suckling, & Bullmore, 2006; Bullmore & Sporns, 2009; Kaiser & Hilgetag, 2006).

In brain imaging, functional magnetic resonance imaging (fMRI) experiments measure groups of neurons as *voxels* (i.e., tiny three-dimensional pixels of brain tissue comprised of neuronal signals), which is the basis for all structural and functional brain connectivity (Glover, 2011). When applied to fMRI data, a historic neuroscientific approach requires analyzing the activation within a few voxel(s) in comparison to a stimulus. The analyses would then determine the specific location of activation in the brain during a particular task. However, the brain operates as a coordinated system; each voxel signal neither activates nor functions in isolation. Rather, each voxel activates and has the potential to connect to each and every other activated voxel throughout the brain

(Sporns et al., 2004). Network techniques capture and measure how the activity of each voxel's signal is related to each and every other voxel signal—as patterns of connectivity—throughout the network. With this approach, comparisons of activity can be made among all voxels throughout the entire brain network (Sporns, Honey, & Kotter, 2007). Network science techniques can capture and measure specific patterns of whole brain activity, thus providing a mathematically robust understanding of the brain as an interconnected system.

There can be both structural and functional brain networks. Structural networks evaluate the structure or morphology of the brain. Their properties provide specific information about the brain's structure and inform how structural connectivity may contribute to functional connectivity. For example, the occipital lobe is a structural region that facilitates vision, while the auditory cortex is an anatomical region that contributes to auditory processing. Structural networks can be morphological brain measurements of *cortical thickness, gray matter volume, surface area,* and *white matter tracts.* Network analyses have revealed that there are differences in structural brain network properties in the brains of people who have schizophrenia and Alzheimer's disease (Bassette et al., 2009), as well as during normal aging and human growth and development (Bullmore and Sporns 2009). Analyses of structural network properties can inform an understanding of functional brain connectivity because structural network differences can impact overall complex brain function (Sporns & Zwi, 2004). For a complete review of structural networks see He and Evans (2010). To put structural networks in the context of brain functional networks, visual or auditory anatomic processing is not visual or auditory perception and cognition (the ability to understand or ‘perceive’ what is seen or heard). Perception and cognition are functions facilitated in the brain. Structural network properties can affect functional networks (i.e., subsequent mental processes or ‘brain function’) (Sporns et al., 2004).

Measurements of functional brain networks (i.e., functional brain connectivity) may be applied to the whole brain using the *BOLD* signal from *fMRI and/*or from *EEG/MEG* data. There are a wide variety of brain functions. A few broad examples are memory, attention and sensory perception (e.g., visual, auditory, and sensory or ‘physical’ sensations). Within each of these broad areas are more specific, finer-grained functions. For example, there is episodic memory, semantic memory, and autobiographic memory to name a few. Each of these broader functions can have numerous sub-functions. For example, for memory function there is memory encoding, memory consolidation, memory retrieval, explicit memory, and declarative memory.

To clarify structural and functional networks further, structural network properties of the cortex of the occipital lobe can impact functional connectivity and influence visual perception. The function of visual perception can also contribute to more complex cognitive functions, as mental operations, that require the structural network properties from frontal regions of the brain. This could be deciding which road to take while driving a car or knowing and chatting with someone who is riding with you in the car. Structural connectivity properties can often determine and influence healthy brain function. Conversely, demands on the functional network, such as the mixture of mental and sensory-motor operational requirements for driving a car, place reciprocal demands on the brain’s structural network properties in order to coordinate successfully the different mental processes for optimal function (Telesford et al., 2011). Due to the constant demands for updating the brain’s operational organization that is potentially required for any mental function, structural connectivity can contribute to dynamic functional connectivity and vice-versa; the two are interwoven and interdependent (Bassett et al., 2009).

Brain Network Measurements

Brain network measurements are statistical procedures applied to brain imaging data for connectivity analyses. Numerous network statistics can be applied to fMRI data. Here is a brief overview and description of the fundamental brain network measurements. A detailed description of these statistics can be found in Rubinov and Sporns (2009).

The most basic of all brain network measurements is *degree,* which measures the number of connection links each voxel (or node) has to other voxels within the brain network. A node that exhibits high degree is a node that has many signal connections to other nodes within the brain network. Nodes are connected to other nodes via links or *edges*. *Path length* is the minimum number of connection stops or ‘steps’ that a node signal requires to reach its target destination within the network. A short path length would suggest efficient brain connections. Efficiency is a measurement of distance signal transfer in the brain. A node with high efficiency tends to be connected to many regions of the brain network. There is both *local efficiency* and *global efficiency*. Local efficiency is a measure of signal information sharing within local regions. High local efficiency implies that nodes tend to share information within their local area. Global efficiency is essentially an inverse measurement of path length. Global efficiency is often used as a measurement of the overall capacity within the brain for parallel information transfer and globally integrated brain network processing (Bullmore and Sporns, 2012). Evidence suggests that global efficiency is an indication of more rapid signal information transfer that can extend to spatially disparate regions of the brain (Bullmore & Sporns, 2009).

Community Structure is a topological partitioning of connections within the network into modules. Modules, also called communities, are subsets of nodes that are densely connected to each other and sparsely connected to other nodes in other modules within the network. Stated more simply, communities are those nodes that share interconnections of densely connected nodes but sparsely held intra-connections within the network. Community structure measures the modularity or 'sub-global organization' of a complex network (Bullmore and Sporns, 2012). Modular networks can be partitioned into sub-component modules. Thus, modules represent stable intermediate states that can evolve by experiencing a change in one module at a time, without risking the loss of function within other modules; well-adapted modules do not jeopardize the function of the entire system (Meunier, D., Lambiotte, R., and Bullmore, E.T., 2010).

Some of the more conspicuous brain network measurements available in the current literature can be viewed in Table 1. These measurements contribute to an increasingly complete understanding of how structural connectivity contributes to dynamic function (Bullmore & Sporns, 2009). Researchers in the field are currently developing new statistical algorithms for investigating and analyzing brain connectivity. Advancements in the field will likely provide new statistical measurements that will provide further insight into brain structure and function.

Network analysis is currently a leading frontier in the highly active area of neuroscience research. A complete and accurate comprehension of different brain states (e.g., developing, healthy, maladaptive, injured, recovering and diseased) is shared by scientists, health professionals, educators, governments and the general public around the globe. Indeed, the quest for a full understanding of the brain is presently considered one of the Grand Challenges of the 21st century. To this end, the fundamental desire for understanding how the brain functions as a system— through the application of network science based methods—is now considered the leading approach within the field of neuroscience (Logothetis, 2008). From this understanding, lasting clinical applications and therapeutic interventions, as well as informed developmental and educational approaches, for the brain can be envisioned.

Table 1

Network Properties

Network property	Definition
Degree	The number of nodes any particular node is connected to within the network.
Assortativity	The correlation between the degrees of connected nodes. The tendency for nodes to be connected to nodes of similar degree.
Edges	Connection links between nodes.
Node	The most fundamental component of any network.
Voxel	A three-dimensional pixel of brain tissue measured with fMRI,
Path length	The number of connection stops a node signal travels to reach its final destination.
Clustering coefficient	The number of connections between the nearest neighbors of a node as a proportion of the maximum possible number of connections. The clustering correlation coefficient is the fraction of connections out of all the possible connections and a measure indicating that a node's neighbors are also neighbors of each other as a measure of cliquishness.
Degree distribution	The degree distribution is the degrees of all the nodes in the network.
Graph	Defined as a set of nodes connected by links as edges.
Modularity	The number of interconnected nodes when compared to outer connections.
Centrality	A class of networks that calculate the varying importance of a node in terms of how many pairs of nodes a signal passes through it within the overall network.
Hubs	Nodes with high degree or high 'centrality' are generally referred to as Hubs.

Network property	Definition
Global efficiency	Nodes that are connected through short path lengths regardless of spatial location.
Betweeness centrality	Nodes that connect between many pairs of otherwise unconnected nodes in the network.
Adjacency matrix	Once the cross correlation is performed, the network is binarized based on a thresholding procedure to reveal the presence or absence of the most highly connected nodes. The presence of a node connection is then given a 1 and those nodes not meeting threshold are given a 0. The result is called the adjacency matrix. Further details, including thresholding procedures, may be found in Chapter 4 and the glossary.

A Default Mode of Brain Function

Advances in understanding the brain's system are frequently found in unexpected ways. Such was the case in the discovery of the *default mode network* of the brain. During routine fMRI experiments, scientists discovered a unique feature about brain function (Raichle et al., 2001). A signal of activity was found to habitually show up in the fMRI *BOLD s*ignal during the *task-negative* component of experiments. In other words, a signal was consistently showing up when the brain was *not* actively engaged in a task. Prior to this discovery, during a typical fMRI experiment, this signal of BOLD activity was considered noise and disregarded; the signal was regressed out of the data analysis as a nuisance parameter. However, based on mounting evidence that this regular observation was not an artifact, but rather, actually a component of correlated signaling between theoretically opposed functional brain regions, this set of spontaneous fluctuations in the fMRI signal was determined to be an underlying aspect of intrinsic resting-state brain function (Buckner, Andrews-Hanna, & Schacter, 2008; Fox et al., 2005; Fox, Zhang, Snyder, & Raichle, 2009; Raichle et al., 2001). For a recent review see Fox and Raichle (2007). This task-negative system, as an intrinsic aspect of signaling within the brain during rest, was termed the "*default mode network*' (Greicius, Krasnow, Reiss, & Menon, 2003).

The default mode network, exhibiting a consistent pattern of underlying signal deactivation during a task, includes disparate regions of the brain such as the precuneus/posterior cingulated cortex (PCC), the medial prefrontal cortex (MPFC), and the medial, lateral, and inferior parietal cortex (Raichle et al., 2001). In particular, the precuneus has been found to have importance to the network (Fransson & Marrelec, 2008). To summarize, the default mode network is an interconnected set of regions in the brain that appears to function cooperatively while a person is awake, but not actively engaged in a task (i.e., at rest). However, far from being merely task-negative, this resting-state default network has been implicated in such intriguing mental functions as self-referential processing, episodic memory, rumination, and mind wandering or day dreaming (Gusnard, Akbudak, Shulman, & Raichle, 2001; Raichle, 2010; Raichle et al., 2001).

The idea that the brain has an underlying functional network running on idle while not engaged in a goal-directed task is intriguing. During childhood development, there is recent evidence that this network becomes more consistent during the maturation process. For example, children between the ages of 9 -12 demonstrate more consistency in non-goal-directed processing when compared with infants and children up to 7 years old (Fair et al., 2008; Fransson & Marrelec, 2008; Thomason et al., 2008). Indeed, new advancements in scientific understanding offer that the default mode network may benefit specific aspects of healthy brain function such as creativity and fluid intelligence (i.e., the ability to make connections and see relationships between previously disparate concepts to generate original thoughts or ideas) (Immordino-Yang, Christodoulou, & Singh, 2012; van den Heuvel, Stam, Kahn, & Pol, 2009).

Equally compelling, disruptions within the default mode network now appear to relate to a host of neurological challenges and mental disorders such as Alzheimer's disease (Greicius, Srivastava, Reiss, & Menon, 2004), autism (Allen, Hill, & Heaton, 2009; Assaf et al., 2010), anxiety and depression (Jin, Pelak, & Cordes, 2012), post-traumatic stress disorder (PTSD), schizophrenia, and attention deficit disorder (for a full review see Broyd et al., 2009). Finally, the default mode network is now implicated in varying levels of mental awareness and consciousness (Fingelkurts, Bagnato, Boccagni, & Galardi, 2012; Jin et al., 2012; Schiff & Fins, 2007). To summarize, while arguing that more research is certainly needed to substantiate these claims, the default mode network now appears to underlie a host of mental states that contribute to maintaining healthy brain function (for a complete review of the default mode network and mental states see (Broyd et al., 2009).

Music and the Brain

The scientific study of music and the brain is an interdisciplinary field that combines knowledge from music, audiology, communication science, neuroscience, cognitive science (i.e., neuropsychology), and brain imaging (i.e., radiology**).** An understanding of the effects of music on the brain is currently an emerging focus of interest from the global scientific community. As an emerging frontier, the terms presently used to describe this interdisciplinary field are *The Cognitive Neurosciences of Music* and *Neuromusicology***.** Research results indicate that listening to music engages a broad and complex set of coordinated processing systems within the human brain (Peretz & Zatorre, 2005b). Researchers have found these activated areas are associated with a diverse range of perceptual and response systems, many of which generate and mediate meaning between the individual and the external world. The brain's capacity to organize and perceive music connects networks associated with time perception, pattern and spatial recognition, physiological and sensory monitoring, as well as functional elements implicated in memory, cognition, mood fluctuation, and emotion (Peretz, 2002; Zatorre, Belin, & Penhune, 2002). Because of these processing systems, research on music and the brain is currently considered fundamental to questions surrounding consciousness, the evolution of language and emotion, and the biological underpinnings of the brain. However, the phenomenon surrounding music and its effects on the brain remains to be fully explored (Ball, 2008; Panksepp & Bernatzky, 2002; Patil, Pressnitzer, Shamma, & Elhilali, 2012; Peretz & Zatorre, 2005; Perlovsky, 2011; Salimpoor et al., 2011). A goal of the present series of studies is to provide an increased understanding regarding the effects of music on the brain.

Emotional Responses to Music

One of the more compelling aspects about music is the effect it appears to have on the human emotional-response system (Juslin & Sloboda, 2001). People choose to listen to music because they want to; music gives them a sense of pleasure or enjoyment. The mental connection between music and emotional responses has been perhaps one of the most intriguing, and yet beguiling, within neuroscientific music research. While a poorly understood brain phenomena, researchers have found that human beings primarily value music for how it makes them feel (Juslin & Vastfjall, 2008; K. Norton, 2011). Whether the music is slow and soothing, or fast and upbeat, people listen to music to change their mood, match their mood, release mental states of emotion, and to relieve stress (Behne, 1997). To state this idea more simply, music apparently influences how people feel (i.e., their mental state). Emotional responses to music are perhaps the most intriguing aspect of neuroscientific music research because they hint at the elusive concept of the power of music. Music appears to elicit powerful emotional and behavioral responses in people (Azoulay, Chaize, & Kentish-Barnes, 2013; Bae, Lim, Hur, & Lee, 2014; Baker & Brown, 2014; Bellieni et al., 2013; Bensimon, Einat, & Gilboa, 2013; Berman, 2001; Bezdek & Gerrig, 2008; Bhunnoo, 2008; Bigliassi, Leon-Dominguez, Buzzachera, Barreto-Silva, & Altimari, 2014; Bjorkman, Karlsson, Lundberg, & Frisman, 2013). There is also the aesthetics question surrounding emotional-responses related to music (i.e., Why is music frequently described as aesthetically pleasing or beautiful?) (Hodges & Sebald, 2011).

Historically, within both philosophy and psychology, the human emotional-response system was considered independent from intellectual purpose (Damasio, 1994). The brain, processing cognition, functioned analogously to a highly developed computerized system. Emotions—personal, intricate, and often perplexing—were viewed as simply problematic, often complicating an otherwise well-functioning mental network of streamlined neurological organization. However, advances in neuroscience combined with brain imaging have disclosed that these two processes are actually fine-grained interdependent systems and much more essential for healthy human functioning than previously recognized (Damasio, 1994; Damasio, 2008; Immordino-Yang, McColl, Damasio, & Damasio, 2009).

Powerful questions surround why responses to music have been shown throughout history to have the ability to motivate, disrupt, or quell human behaviors. Yet, harnessing the power of music in order to channel it for human benefit requires a full understanding of the effects of music on the brain (Zatorre & McGill, 2005). Consequently, understanding the mechanisms that contribute to the curious effects that music appears to have on responses in the brain is of interest. Understanding the underlying mechanisms that contribute to emotional responses to music may provide an enhanced understanding of the biological origins of music and the mental-emotional system of the brain. Furthermore, such an understanding may begin to help explain the wide variety of successful results being found from the application of music in both clinical and educational environments (Bergstrom, Seinfeld, Arroyo-Palacios, Slater, & Sanchez-Vives, 2014).

Within the brain, emotional responses to music appear to engage multiple regions implicated in reward and emotion, such as the limbic and paralimbic regions, the insula, and the striatal system including the caudate and nucleus accumbens (Blood & Zatorre, 2001; Blood et al., 1999; S. Brown, Martinez, & Parsons, 2004; Koelsch, 2010; Mavridis, 2014; Salimpoor et al., 2011). While the musical stimuli in these experiments were limited (i.e., a few chords, tones, or brief excerpts), these studies suggest that comprehending emotional-responses to music may contribute to more complete understanding of evolutionary neurobiological systems.

Music and Preferences

Human beings typically prefer specific styles of music. Due to the outstanding evolutionary and biological questions surrounding ‘why music’ and the effect of listening to music related to emotion and behavioral responses, research on music preferences is currently an active area of inquiry (Bigerelle & Iost, 2000; Brattico, Bogert, & Jacobsen, 2013; R. A. Brown, 2012; Ornes, 2014; Peretz, Gaudreau, & Bonnel, 1998; Ter Bogt, Keijsers, & Meeus, 2013). Understanding preferential music has led to the study of characteristics of music related to human perceptions of aesthetics or beauty (Bigerelle & Iost, 2000; Bonneville-Roussy, Rentfrow, Xu, & Potter; Hsu & Hsu, 1991; Hsu & Hsu, 1990). From the research, we know that music preferences are developed during the lifespan, are often contextually situated (e.g., a party or a funeral) (Blumstein, Bryant, & Kaye; Brattico & Jacobsen, 2009; Cross, 2012; Fritz, Schmude, Jentschke, Friederici, & Koelsch, 2013), and are generally influenced by a host of different age, cultural, and environmental, factors related to exposure (Chapin, Jantzen, Kelso, Steinberg, & Large, 2010; Juslin & Vastfjall, 2008; Rentfrow & Gosling, 2003; Schafer, Tipandjan, & Sedlmeier, 2012). Thus, discovering how the brain deciphers preferential music—as a musically driven emotional-response system—may help to unlock how the mind experiences aesthetically satisfying experiences.

Interest in applications from an understanding of musical preferences is shared by evolutionary biologists, archeologists, educators, physicians, therapists, machine learning scientists, retailers, film and music industry specialists, the video gaming industry, and producers of commercial children's programming. In brief, fundamental preference for consonant music appears to be found in preborn and newborn infants (Partanen, Kujala, Tervaniemi, & Huotilainen, 2013; Trehub, 2003; Virtala, Huotilainen, Partanen, Fellman, & Tervaniemi, 2013). While exposure plays a role in the development of musical preferences, as a biological phenomenon, these results suggest that preferences in music may have more of a basis from nature, rather than nurture. However, the phenomenon of musical preferences appears to be culturally diverse and dynamically attached to a wide variety of mental and emotional states (Ball, 2008; Edwards, 2007; Egermann, Grewe, Kopiez, & Altenmuller, 2009; Eldar, Ganor, Admon, Bleich, & Hendler, 2007; Fritz et al., 2009; Istok, Brattico, Jacobsen, Ritter, & Tervaniemi; Sloboda, 2008). Yet, curiously enough, people report that listening to strongly preferred music—regardless of the type—is often deeply satisfying and can frequently generate introspective thoughts and personal memories (Gabrielsson & Bradbury, 2011). Thus, how listening to different types of preferential music can spontaneously trigger similar types of mental responses of self-reflective thought and emotionally-laden memories across human beings remains an open question.

CHAPTER III

EXPERIMENT ONE: NETWORK SCIENCE: A NEW METHOD FOR INVESTIGATING THE COMPLEXITY OF MUSICAL EXPERIENCES IN THE BRAIN

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Chapter III was published in *Leonardo Transactions* (2011) and is reprinted here with permission. Stylistic variations and layout are due to requirements of the journal. The article, however, has been modified from its original published version to create a consistent formatting style throughout the document for in-text citations and references. Robin W. Wilkins conceived, designed and performed the experiments. Robin W. Wilkins processed and analyzed the data and prepared the manuscript. Paul J. Laurienti and Jonathan H. Burdett supervised the data analysis and preparation of the manuscript. Matthew R. Steen supervised the data processing procedures. Donald A. Hodges acted in an advisory and editorial capacity.

Abstract

Network science is a rapidly emerging analysis method for investigating complex systems, such as the brain, in terms of their components and the interactions among them.

Within the brain, music affects an intricate set of complex neural processing systems. These include structural components as well as functional elements such as memory, motor planning and execution, cognition, and mood fluctuation. Because music affects such diverse brain systems, it is an ideal candidate for applying network science methods. Using as naturalistic an approach as possible, we investigated whether listening to different genres of music affected brain connectivity. Here we show that varying levels of musical complexity affect brain connectivity. These results suggest that network science offers a promising new method to study the dynamic impact of music on the brain.

Introduction

Network science has emerged as a method that offers a useful framework for capturing and studying complex systems (Watts & Strogatz, 1998). Based on graph theory, network science measures complex system properties and quantifies the relationships among network property components (Barabasi & Albert, 1999). There is arguably no more complex biological system for investigation than the human brain. The brain exhibits characteristics of small-world connectivity with regional specificity manifesting through high local clustering and distributed information via short path-lengths. The ability to study how the brain behaves and functions as an integrated system offers the opportunity to pursue new research questions while advancing the knowledge of both structural and functional connectivity (Bullmore & Sporns, 1999).

Brain Networks vs. Brain Activations

Using network methods to study the brain is different from traditional neuroscience imaging. In traditional neuroscience, scientists typically administer a task and measure specific activation areas within the brain relative to the given task: what turns "on" in the brain while performing the task. This traditional method requires the experiment to be extremely narrow in scope to accurately measure activation site(s). However, the brain does not activate areas in static isolation. Rather, the brain functions as a cohesive whole and, therefore, as a network. We are interested in how the entire brain network changes across tasks. We also study the effects of each brain area on every other brain area within the network during a specific task. There are a multitude of metrics one can use to measure and analyze brain connectivity: degree distribution, community structure, local and global efficiency, centrality, and path length, for example. Each of these metrics provides a layer of information to help us determine brain connectivity. This kind of analysis may therefore help us understand how structural brain connectivity contributes to functional connectivity and reveals the consistency of networks across people. We have chosen in this manuscript to focus on the network metric degree, often denoted K. Degree is the number of edges that connect to each node (i). Thus, the degree of a node is the number of connections that node has within the network. Network analyses can be used to determine the degree in every voxel in the brain. In the brain, when a node is said to have high degree, it functions similar to what we might consider a brain communication center or "hub". Hubs are regions considered critical for network integrity. If damaged, these hubs dramatically alter information processing over the entire network (Sporns et al., 2007). Nodes ranked in the top 10-20% of the brain's node degree distribution within the network are generally considered hubs. Using this metric one can determine how consistently brain hubs are represented across people, that is, the typical location or region of hubs. We report in this manuscript the consistency of brain hubs across people when undergoing different musical experiences.

The Human Musical Experience

Perhaps more than any other externally orchestrated stimuli, music remains singularly one of the most mysterious perceptive experiences within the complexity of the human mind. From the time of ancient Greek philosophers, such as Aristotle, to contemporary thinkers, speculations about why music exists, much less why humans of all cultures and throughout time, are willing to spend so much time engaged with music, continue to intrigue both the philosophic and scientific communities (Perlovsky, 2010). Researchers from such diverse disciplines as machine learning, physics, anthropology, and philosophy consider music to be one of the most complex aspects of the universal human experience (Mithen, 2006; Panksepp & Bernatzky, 2002; Hodges & Sebald, 2011; Zatorre, 2005).

Within the brain, research has shown that music connects a diverse set of intricate neural processing networks. These complex networks are associated with sensory and motor processing, cognition, memory, and mood or emotional fluctuation (Zatorre & Peretz, 2001). Music has been revealed to influence speech and language development, brain plasticity, spatial reasoning, the mirror-neuron system and clinical health recoveries (Peretz & Robert, 2005; Schlaug, 2009a). Additionally, music has been included at the center of provocative questions surrounding the emergence of consciousness, emotions and theory of mind (Schlaug, 2009b; Livingstone & Thompson, 2009; A.R. Damasio, 1999). However, many questions remain. Research into the connections and potential contributions music offers for understanding these questions remains largely unexplored (Ball, 2008). Studying how the brain is affected by music- as people actually experience it- has proved immensely challenging. Previous fMRI (functional magnetic resonance imaging) and PET (positron emission tomography) studies have often been structured around tones, chords or brief excerpts. These imaging experiments required time constraints for appropriate scientific analysis. However, music listening is more than a single or multi-second event. When people listen to music, their response occurs over time. Imaging studies not able to account for that lose valuable information. Now, with the grounding of network science methodology, metrics are available to apply and study promising questions within neuroscience. This study sought to answer whether brain connectivity is altered when listening to different genres of music. Network connectivity was studied resulting from listening to a series of songs from different genres having varying musical complexity.

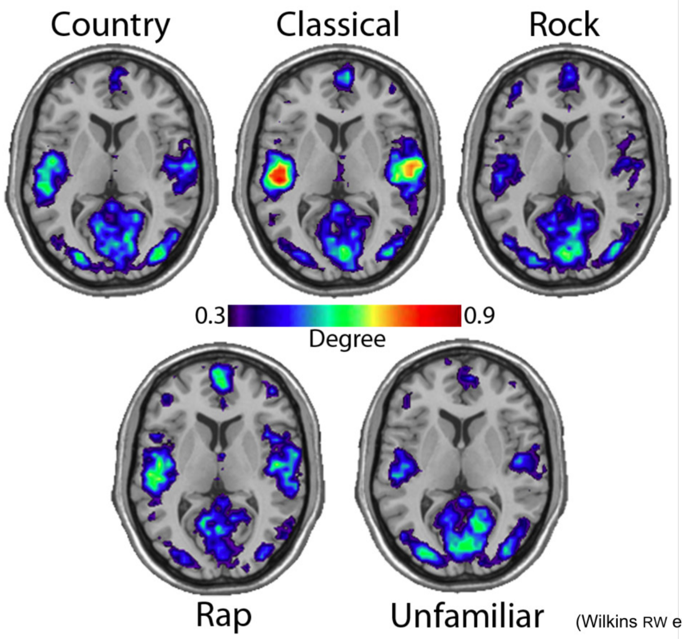
Brain Imaging Methodologies

We performed network generation and analysis using the fMRI time series data acquired from 21 subjects while listening to music with their eyes closed. We selected songs that would be considered iconic within the music genre repertoire. Songs included Water, by Brad Paisley, (country), Mvt I Symphony No. 5 by Beethoven (classical), Rock and Roll All Nite by Kiss (rock), OMG by Usher (rap), and Spring Hall by the Chinese

Jinna Opera Band (unfamiliar). Each of the songs was played continuously for five minutes and presented in pseudo-randomized order.

Whole-brain connectivity was evaluated using graph theory methods on a voxel-by-voxel basis. Voxel-by-voxel analysis allows for each voxel (or node) to be counted and considered within the context of the overall brain network (Hayasaka & Laurienti, 2010).

In summary, an adjacency matrix (A*ij*), or whole-brain connectivity matrix, was generated for each subject. This is a binary *n x n* matrix, where *n* = the total number of brain voxels, with each voxel representing a network node (~21,000 in these data). The matrix defines the presence or absence of a node connection between any two nodes (*i* and *j)*. The adjacency matrix serves as the basis for most of the network analysis.



(Wilkins RW et al 2011)

Figure 9. The Auditory Cortex and Music Genres. These images show the consistent location of hubs for each of the genres in the brain. An axial slice at the level of the auditory cortex for power spectral density is depicted.

For the fMRI data, the determination of a connection between any two nodes (i and j) was performed using a time series regression analysis on spatially normalized brain images. To account for physiological noise associated with cardiac, respiratory and cerebrospinal fluid changes, our fMRI time series was first band-pass filtered (0.009-0.08 Hz). A full regression analysis was performed including motion parameters as well as global, white matter, and CSF covariate of no interest to further correct for physiological noise. This produced a cross-correlation matrix that contained the partial correlation coefficient representing the connectivity between each and every node (for details see Joyce et al., 2010). An adjacency matrix was generated for each subject by thresholding the correlation matrix as described in (Hayasaka & Laurienti, 2010).

Brain Imaging Network Results: Does Musical Genre Really Matter?

Findings indicate that when listening to different genres of music, the brain exhibits different connectivity patterns and hub locations. Specifically, the brain exhibited a higher degree (*K)* within the auditory cortex when listening to classical music [Figure 9] compared to the other musical genres. Interestingly, when listening to other musical genres, the auditory cortex was not as highly connected. This high degree of connectivity within the auditory cortex is arguably the result of the greater complexity within the structure of the classical music.

Future Directions

While the degree within the auditory cortex is different between the genres, the response within the overall brain network is likely affected by musical preference. Future analyses might reveal how brain connectivity is altered by *personal preference*, including whether overall personal preference, regardless of genre, affects brain connectivity. In addition, further network analyses on these data will use network methodology to identify brain network neighborhoods as a function of musical genre and musical preference.

Methods

Twenty-one young adults (average age 24 ± 3.4 yrs) were recruited based on their favorite musical genre: classical ($n = 5$), country ($n = 5$), rap/hip hop ($n = 5$), and rock music ($n = 6$). All participants were right-handed, English speaking, color-sighted, had normal hearing and were free from neurological disorders. Participants were recruited by flyer and word of mouth and signed Informed Consent documents approved by the Wake Forest Baptist Medical Center Institutional Review Board. Prior to scanning, participants completed a comprehensive questionnaire about formal musical training, personal use of music, and a preference ranking of a total of eleven music genres, (classical, country, gospel/blues, rap/hip hop, alternative, rock, Christian, folk, pop, metal, Broadway, jazz, classic rock), as well as identification of their top favorite song. Ten subjects reported as having formal musical training. Eight had completed, or were in the process of completing, a university music degree. Eleven reported that they could read music fluently.

Stimuli

Six musical selections, hereafter referred to as songs, were presented randomly to each participant in the MRI scanner while blood oxygen level dependent (BOLD) functional MRI (fMRI) data were collected. The six songs, each five minutes long, included four pre-selected songs considered iconic within each musical genre, an unfamiliar selection, and a sixth personal favorite song. The five songs presented to every subject were Movement I from Symphony No. 5 by Beethoven (classical genre), “Water” by Brad Paisley (country genre), “OMG” by Usher (rap /hip hop genre), “Rock ‘N Roll All Nite” by KISS (rock genre), and “Spring Hall” by the Chinese Jinna Opera Band (unfamiliar genre).

Network Generation and Analysis

Network generation and analysis was performed using the fMRI time series data from each subject with eyes closed. To account for physiological noise associated with cardiac, respiratory and cerebrospinal fluid (CSF) changes, the fMRI time series was first band-pass filtered (0.009-0.08Hz). The full regression analysis was then performed including motion parameters, as well as global, white matter, and CSF covariates of no interest to further correct for physiological noise. For the fMRI data, the determination of a voxel connection between *i* and *j* was performed using a time-series regression analysis on spatially normalized brain images. This analyses produced a cross-correlation matrix containing the partial correlation coefficient representing the strength of connections between each and every network node (~21,000 in these data). In order to compare networks across people, the network was defined such that the relationship between the number of nodes and the average node degree (K) was the same across different subjects. In particular, the network was defined so that $S = \log(N)/\log(K)$ was consistent across subjects. This relationship was based on path length of a random network with N nodes and average degree K (Stam & Reijneveld, 2007; Supekar, Menon, Rubin, Musen, & Greicius, 2008) and can be re-written as $N = K^S$.

To measure the most highly connected nodes, a threshold is required. Based on previous research, similarly sized matrices with thresholds set at 2.0-3.0 show less inter-subject metric fragmentation and variability (Burdette et al., 2010). To capture the highest degree of connectivity, therefore, a threshold of 2.5 was applied to the matrix, resulting in the binary adjacency matrix (A_{ij}). Once the complete adjacency matrix was generated for each subject, network metrics were calculated. To measure the overall topological feature of the brain network across our subjects under the three conditions whole-brain mean values were first calculated. This measure indicates the nodal values that can then be averaged across the entire network. Reported metrics were subsequently calculated and mapped back into 3D brain space, with each voxel corresponding to the number of subjects having a particular node metric at a specific voxel location (coordinate) and visually depicted using top overlap maps.

A detailed description of the metrics calculated in this study may be found in the review work of Rubinov and Sporns (2010). Network generation and analyses were performed for each participant using the fMRI time series from each subject's musical experiences. Out of the songs, reported here are the network results for the consistency across the subjects from the five pre-selected genres. Network calculations and analyses, therefore, were conducted based on the iconic music genre selections. The consistency of brain networks across all subjects was depicted based on these conditions.

For the network analyses, whole-brain connectivity was evaluated using voxel-based graph theory methods (Hayasaka & Laurienti, 2010; Joyce et al., 2010). The most fundamental network science property is degree. Degree (*K)* is the primary measurement of brain connectivity because it measures the number of edges or functional links for each node in the network. Determined by the number of neighbors connected to node *i*, degree calculates the number of edges that each node *i* has with N number of nodes. For each subject, a degree distribution was measured under each condition. These distributions show the degree of each node plotted against 1 minus the cumulative distribution (Hayasaka & Laurienti, 2010). Nodes ranked in the top 20% of the brain's degree distribution within a network are generally considered 'hubs.' In the brain, when a node has high degree, it functions as a brain communication center or hub. Hubs are considered critical for network integrity. If damaged, these hubs dramatically alter information processing within the entire network (Bullmore & Sporns, 2009). In the 3D image, hubs were identified as the most connected nodes across subjects and visually represented by peak height (see Figure 9 in Results).

Network generation and analysis was performed using the fMRI time series data acquired from 21 subjects while listening to music with their eyes closed. Songs were selected that would be considered iconic within the music genre repertoire. Songs included "Water" by Brad Paisley (country), Movement I of Symphony No. 5 by Beethoven (classical), Rock and Roll All Nite by Kiss (rock), OMG by Usher (rap), and Spring Hall by the Chinese Jinna Opera Band (unfamiliar). Each of the songs was played continuously for five minutes and presented in pseudo-randomized order. Whole-brain connectivity was evaluated using graph theory methods on a voxel-by-voxel basis. Such analysis allowed for each voxel (or node) to be counted and considered within the context of the overall brain network (Hayasaka & Laurienti, 2010).

In summary, first an adjacency matrix (A*ij*) was generated, or whole-brain connectivity matrix, for each subject. This matrix is a binary *n x n* matrix, where *n* = the total number of brain voxels, with each voxel representing a network node (~21,000 in these data). The *Aij* matrix defines the presence or absence of a node connection between any two nodes (*i* and *j)*. The adjacency matrix serves as the basis for most of the network analysis.

For the fMRI data, the determination of a connection between any two nodes (i and j) was performed using a time series regression analysis on spatially normalized brain images. To account for physiological noise associated with cardiac, respiratory and cerebrospinal fluid changes, the fMRI time series was first band-pass filtered (0.009-0.08 Hz). A full regression analysis was then performed including motion parameters as well as global, white matter, and CSF covariate of no interest to further correct for physiological noise. This analysis produced a cross-correlation matrix that contained the partial correlation coefficient representing the connectivity between each and every node. For details see (Joyce et al., 2010). An adjacency matrix was generated for each subject by thresholding the correlation matrix as described in Hayasaka and Laurienti (2010).

Results

Results revealed that when listening to different genres of music, the brain exhibits different connectivity patterns and hub locations. Specifically, the brain exhibited a higher degree (*K)* within the auditory cortex when listening to classical music [Figure 9] compared to the other musical genres. Interestingly, when listening to other musical genres, the auditory cortex was not as highly connected. This high degree of connectivity within the auditory cortex is arguably the result of the greater complexity within the compositional structure of the classical music.

Conclusions

In this chapter, the focus was on the network metric *degree*, often denoted *K*. Degree was the number of edges that connect to each node (*i*). Thus, the degree of a node was the number of connections that it had within the network. Network analyses were used to determine the degree in every voxel in the brain. In the brain, when a node had a high degree, it functioned similar to what might considered a brain communication center or 'hub.' Hubs are regions considered critical for network integrity. If damaged, these hubs dramatically alter information processing over the entire network (Sporns et al., 2007). Nodes ranked in the top 10-20% of the brain's node degree distribution within the network are generally considered hubs. Using this metric determined how consistently brain hubs were represented across people, i.e., the typical location or region of hubs. This chapter showed the consistency of brain hubs across people when undergoing different musical genre listening experiences.

CHAPTER IV

EXPERIMENT TWO: NETWORK SCIENCE AND THE EFFECTS OF MUSIC PREFERENCE ON FUNCTIONAL BRAIN CONNECTIVITY: FROM BEETHOVEN TO EMINEM

R. W. Wilkins, P. J. Laurienti, D. A. Hodges, M. R. Steen, & J. H. Burdette

Chapter IV was published in *Nature Scientific Reports* on August 28, 2014 and is reprinted here with permission. Stylistic variations and the layout of the article are due to requirements of the journal. Additionally, the article has been modified from its original published version to create a consistent formatting style throughout the document for in-text citations and references. Robin W. Wilkins conceived and conducted the experiments, processed and analyzed the data and prepared the manuscript and supplementary manuscript. Paul J. Laurienti supervised the data analysis and assisted in the writing and editing of the manuscript and supplemental material. Matthew R. Steen assisted in processing the data and supervised the data processing procedures. Donald A. Hodges and Jonathan H. Burdette acted in an advisory and editorial capacity.

Abstract

Most people choose to listen to music that they prefer or like such as classical, country or rock. Previous research has focused on how different characteristics of music (i.e., classical versus country) affect the brain. Yet, when listening to preferred music regardless of the type—people report they often experience personal thoughts and memories. To date, understanding how this occurs in the brain has remained elusive. Using network science methods, we evaluated differences in functional brain connectivity when individuals listened to complete songs. We show that a circuit important for internally focused thoughts, known as the default mode network, was most connected when listening to preferred music. We also show that listening to a favorite song alters the connectivity between auditory brain areas and the hippocampus, a region responsible for memory and social emotion consolidation. Given that musical preferences are uniquely individualized phenomena and that music can vary in acoustic complexity and the presence or absence of lyrics, the consistency of our results was unexpected. These findings may explain why comparable emotional and mental states can be experienced by people listening to music that differs as widely as Beethoven and Eminem. The neurobiological and neurorehabilitation implications of these results are discussed.

Introduction

Listening to music affects an intricate set of complex processing systems in the brain (Zatorre, 2003), such as systems associated with sensory-motor processing as well as functional elements implicated in memory, cognition and emotion or mood fluctuation (Blood & Zatorre, 2001; Blood et al., 1999; Menon & Levitin, 2005; Schlaug et al., 2011). Listening to music often connects thoughts and emotions and, therefore, is associated with questions surrounding consciousness and “Theory of Mind” (the ability to understand the intentions and emotional state of others) (A. Damasio, 1999; Jackendoff

& Lerdahl, 2006; Perlovsky, 2010). However, little is understood about how listening to music affects the brain (Ball, 2008; Cross, 2003; Gabrielsson & Bradbury, 2011).

One of the most challenging neuroscientific questions surrounding the phenomenon of music preferences is how listening to different types of music can connect the same brain systems (i.e. similarly experienced circuits in the brain) associated with thoughts and memories (Juslin & Sloboda, 2001). People primarily choose to listen to music that they like (Rentfrow & Gosling, 2003; Salimpoor, Benovoy, Longo, Cooperstock, & Zatorre, 2009), such as country, rock or classical. When listening to strongly preferred music, people report they often experience deeply personal, often unsolicited and emotionally-laden, thoughts and memories (Janata, 2009). Listeners describe that the phenomenon of self-referential thoughts and memories can be triggered by different types of music and the presence or absence of lyrics (Brattico et al., 2011). However, music listening preferences are highly individualized and culturally diverse (Barrett et al., 2010; Juslin & Vastfjall, 2008), and different types of music can vary substantially in their melodic and harmonic features and rhythmic complexity (Wilkins et al., 2012). What remains unanswered is why listening to different types of music can generate similar experiences within the brain. To date, it remains unclear how listening to different types of music can generate these types of similar brain experiences across various individuals (Juslin & Vastfjall, 2008).

Network science is a rapidly emerging and promising analysis method for investigating complex systems in terms of their elements and the relationships and interactions between the network elements (Bassett & Bullmore, 2006; Bullmore &

Sporns, 2009; Rubinov & Sporns, 2010). The recent advent of studying the brain as a complex system offers a fuller understanding of brain organization and function (Bassett & Bullmore, 2009; Bassett & Gazzaniga, 2011). We applied network science techniques to determine whether certain brain patterns of functional connectivity might be associated with an individual's musical preferences. Network science methodological advances offered us the opportunity to simulate more real-world music listening experiences for our participants (Rubinov & Sporns, 2010). Similar to recent efforts to evaluate ecological aspects of music listening (Alluri, Toiviainen, Jaaskelainen et al., 2012; Alluri, Toiviainen, Lund et al., 2013; Burunat, Alluri, Toiviainen, Numminen, & Brattico, 2014; Cong et al., 2014; Toiviainen, Alluri, Brattico, Wallentin, & Vuust, 2014), a specific characteristic of this investigation was that our functional imaging data were collected while people listened to complete songs from the following genres: classical, country, rap, rock, Chinese opera, and a participant's pre-reported favorite song. As an investigation into the under-explored area of musical enjoyment, we applied network science techniques to brain imaging data gathered while people listened to entire songs in an uninterrupted fashion.

Our first analyses sought to identify functional connectivity changes based on the genre or type of music (Wilkins et al., 2012). Here we investigated how listening to preferred music, naturally associated with introspective thought, emotion, and memory, affected functional brain connectivity patterns compared to music that was not preferred. The fact that comparisons were based on individual listening preferences meant that various preferential genres were presented. In order to differentiate between music preference and potential brain networks responding to an individual's personal favorite song, we also evaluated brain responses to each participant's pre-reported favorite song as a separate condition. From this, we were able to determine brain connectivity during the preferred, non-preferred, and favorite conditions.

Results

Music Preference and Brain Networks

We evaluated brain networks from functional magnetic resonance imaging (fMRI) data collected while 21 people listened to five iconic musical selections from different pre-chosen genres and their personal favorite song that was self-reported during their pre-study screening. During the scanning session, participants rated each of the musical selections using a sliding scale to indicate how much they liked the song (see Methods). Whole-brain voxel-based functional networks were created for each participant's three reported conditions: most preferred song, least preferred song (i.e., *liked* and *disliked*), and a pre-reported favorite song. Brain networks were created using each imaging voxel as a network node, and correlation analyses identified network connections. The cross-correlation matrix was thresholded to yield a binary network with a 1 indicating a connection between voxels, or nodes, and a 0 indicating the absence of a connection. Our results show the consistency of brain networks (Moussa et al., 2011; Rubinov & Sporns, 2010) across the participants based on the three reported conditions. Here, we focus on four basic network science statistics: degree, global efficiency, local efficiency and modularity or "community structure" (for a detailed explanation see Methods and Supporting Information).

Default Mode Network and Music Listening

A fundamental measurement of brain connectivity is degree (K), which represents the number of edges or functional links for each node within the brain network (Rubinov & Sporns, 2010). Our results indicated that across study participants high degree nodes, or hubs, were located in the default mode network (DMN) (Raichle et al., 2001) generally, and within the precuneus particularly, regardless of song preference (Figure 10, arrows). The DMN is known to support functional brain states, such as the reprocessing of memories and introspection (i.e. self-referential thoughts) (Gusnard et al., 2001) . Statistical comparisons within the precuneus showed that degree did not differ significantly across conditions (mean degree ± S.D: Like = 53.94 ± 0.39; Dislike = 54.06 ± 0.33; Favorite = 53.95 ±0.48; F(1, 20) = 1.10, p = 0.34); however, the precuneus was a hub relative to the rest of the brain.

Global Brain Efficiency and Music Preference

Despite the precuneus being a hub regardless of preference, there were significant differences in global efficiency in the precuneus for the different conditions. Global efficiency is a surrogate measure of path length, or the number of steps connecting a node to the rest of the functional network nodes. Higher global efficiency indicates fewer steps to reach the rest of the network and may be associated with an increased ability to rapidly combine information across distributed brain regions. Mean global efficiency ± S.D in the precuneus was: Like = 0.206 ± 0.018; Dislike = 0.194 ± 0.018; Favorite = 0.203 ± 0.017; F(2, 17) = 3.58, $p = 0.04$. Global efficiency was significantly higher in the precuneus during the Liked music condition compared to the Disliked condition ($p =$

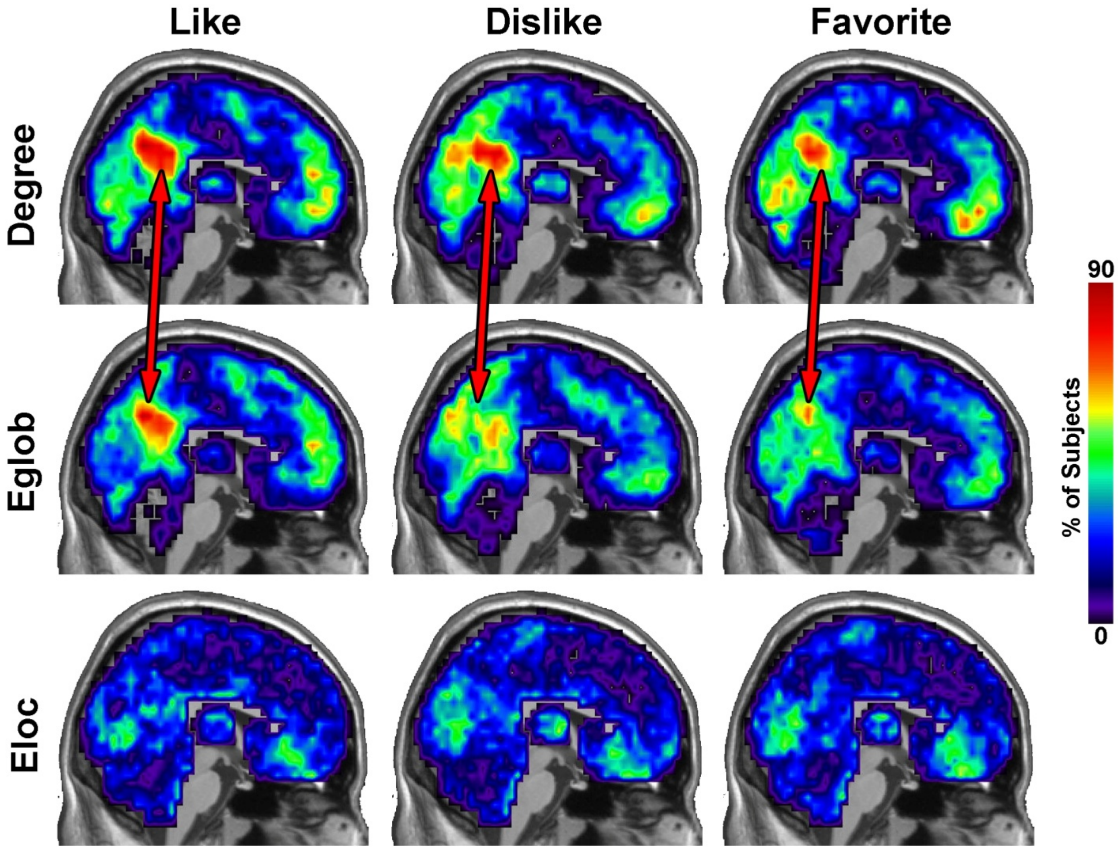


Figure 10. Demonstration of Degree, Global Efficiency and Local Efficiency in the Precuneus. The precuneus exhibited consistent high degree across participants regardless of music preference. Despite being a high degree hub, compared to the like condition, the precuneus showed relatively lower global efficiency in the dislike and favorite conditions. The precuneus has relatively low local efficiency, and there was no difference across the 3 conditions. The scale depicts the percentage of subjects that has a top 20% node in each area for all three network statistics.

Despite the precuneus being a hub regardless of preference, there were significant differences in global efficiency in the precuneus for the different conditions. Global efficiency is a surrogate measure of path length, or the number of steps connecting a node to the rest of the functional network nodes. Higher global efficiency indicates fewer steps to reach the rest of the network and may be associated with an increased ability to rapidly combine information across distributed brain regions. Mean global efficiency ± S.D in the precuneus was: Like = 0.206 ± 0.018; Dislike = 0.194 ± 0.018; Favorite = 0.203 ± 0.017; F(2, 17) = 3.58, *p* = 0.04. Global efficiency was significantly higher in the precuneus during the Liked music condition compared to the Disliked condition (*p* = .017). There was no significant difference in global efficiency between the Liked music and the Favorite music condition (*p* = .330), nor between Favorite and Disliked music (*p*= .132). Figure 10 pictorially depicts the consistency of the brain location for global efficiency (Eglob) across subjects. Comparisons of local efficiency, a measure of local clustering, showed no significant differences between the 3 conditions. Local efficiency values were 0.721 for Like, 0.723 for Dislike, and 0.717 for Favorite, with no p-values less than 0.32.

Network nodes that have high degree tend to have high global efficiency. The fact that the precuneus was found to be a ‘hub’ with high degree regardless of musical preference, but that there were significant differences in global efficiency between Liked and Disliked music, led to a more detailed exploration of precuneus connectivity. Given similar number of connections but different global efficiency indicates that there must be differences in the regions to which the precuneus is connected. A community structure analysis was performed to determine to which nodes the precuneus was most closely functionally connected during the Like, Dislike, and Favorite conditions. Community structure identifies the organization of the network by measuring those nodes that are more highly connected *to each other* than to other nodes in the brain network (thus forming a so-called functional neighborhood). Our results indicate that listening to liked or favorite music affected the community structure differently than disliked music (Figure 11). For details on the methodology, see Methods and Supporting Information.

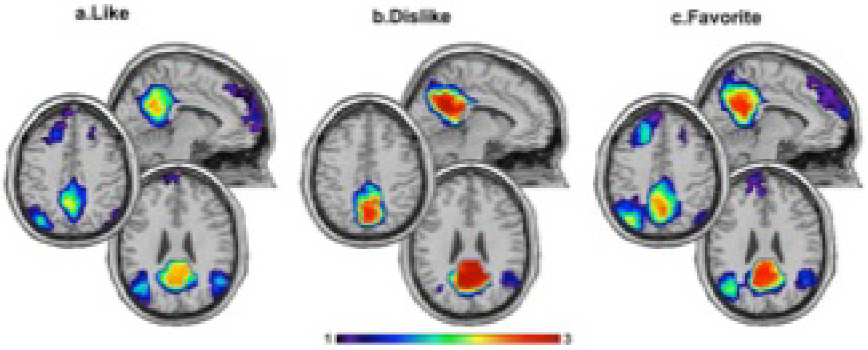


Figure 11. Differences in the Structure of the Pecuneus Community Depending on Music Preference. Demonstration that there are differences in the structure of precuneus community within the default mode network depending on music preference In the Liked and Favorite condition, the precuneus was consistently interconnected with lateral parietal and medial prefrontal cortex (a and c). When the music was disliked, the precuneus was relatively isolated from the rest of the default mode network (b.). Color indicates the consistency of community structure for each voxel across subjects as assessed using scaled inclusivity (see Methods and Supporting Information).

Default Mode Community Structure Differences and Preferential Music

When listening to liked and favorite music, the precuneus community included all regions of the DMN (i.e., precuneus, lateral parietal, and medial frontal cortices) (Figure 11a and c). However, the precuneus community was different when listening to the most disliked song. Specifically, when listening to disliked music, the precuneus dissociated from the medial frontal cortices and was connected primarily only to itself (Figure 11b). This was the most consistent finding in the community structure analysis. In a small portion of the study participants, the precuneus did belong to a community with the lateral parietal lobes as noted by the dark blue regions, but the data clearly demonstrated that the medial frontal portion of the DMN was isolated from the precuneus when listening to music that was disliked. Due to the complexity and multivariate nature of community structure measures and the fact that the consistency metric, scaled inclusivity, yields a single value for the entire population, it is currently not possible to perform traditional hypothesis tests to statistically compare the conditions. However, a *post-hoc* analysis was performed to measure the connectivity between the precuneus and the remainder of the DMN. The results showed a significant ($p = 0.04$) increase in connectivity in the Like condition compared to the Dislike condition. There was no significant difference between Like and Favorite ($p = 0.08$) or between Dislike and Favorite ($p = 0.71$). Details of the analysis methods and specific results including the number of connections measured are presented in the Supporting Information.

Auditory Cortex and Preferential Music: Global Efficiency

The second major investigation in this study involved the auditory cortex, not surprisingly, given the auditory-specific nature of this study. Figure 12 is analogous to Figure 10 in that the degree, global efficiency, and local efficiency of the auditory cortex is depicted. As expected, auditory cortex in the superior temporal region is a hub for liked, disliked, and favorite music. Mean degree ± S.D in auditory cortex was: Like = 88 ± 39; Dislike = 73 ± 48; Favorite = 76 ± 51, and there were no significant differences among degree for the 3 conditions (Like vs. Dislike, *p*=.09; Like vs. Favorite, *p*=.20; Dislike vs. Favorite, *p*=.78). As degree and global efficiency are typically coupled, it was again surprising to find the significantly higher global efficiency in the auditory cortex when listening to the liked song compared to Dislike and Favorite (Like vs. Dislike, *p*=.002; Like vs. Favorite, *p*=.016; Dislike vs. Favorite, *p*=.35). Mean global efficiency ± S.D in auditory cortex was: Like = 0.21 ± 0.02; Dislike = 0.19 ± 0.02; Favorite = 0.2 ± 0.02. As observed in the precuneus, there were no significant differences in local efficiency among the three conditions and is not discussed further.

Community Structure and Favorite Music: Hippocampus and Memory

Given this dissociation between Eglob and degree in the auditory cortex, a community structure analysis was again performed to determine the auditory neighborhood. In the Like and Dislike conditions, the auditory cortex community included the hippocampi, a region recognized to be associated with memory consolidation (Figure 13a). However, in the Favorite condition, the hippocampus functionally separated from the auditory cortex, with the hippocampus becoming its own distinct community (Figure 13b). Although the consistency of the hippocampus was relatively low compared to auditory cortex, it clearly belonged to an isolated community in the Favorite condition. The auditory cortex had disengaged from the hippocampus despite the varied presence or absence of text (lyrics) and acoustic complexity of the personal favorite musical selections.

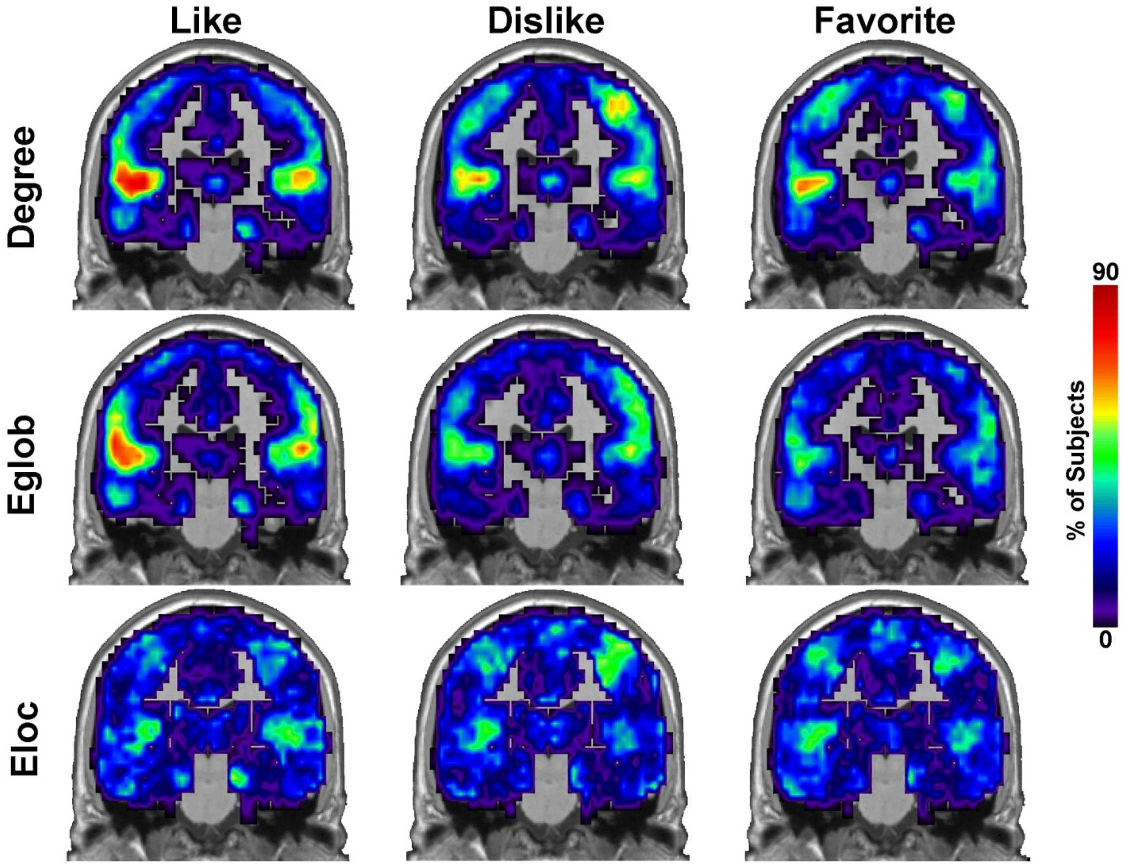


Figure 12. Demonstration of Degree, Global Efficiency, and Local Efficiency in the Auditory Cortex. The auditory cortex was a focus of high degree nodes in all three conditions. Although consistency is visually highest in the Liked condition, there were no significant differences among the three conditions. As observed in the precuneus, the global efficiency was consistently high in auditory cortex only in the Liked condition. Though there are obvious foci of high local efficiency nodes in the auditory cortex, the consistency was lower than other network statistics, and there were no differences among the 3 conditions. The scale depicts the percentage of subjects that has a top 20% node in each area for all three network statistics.

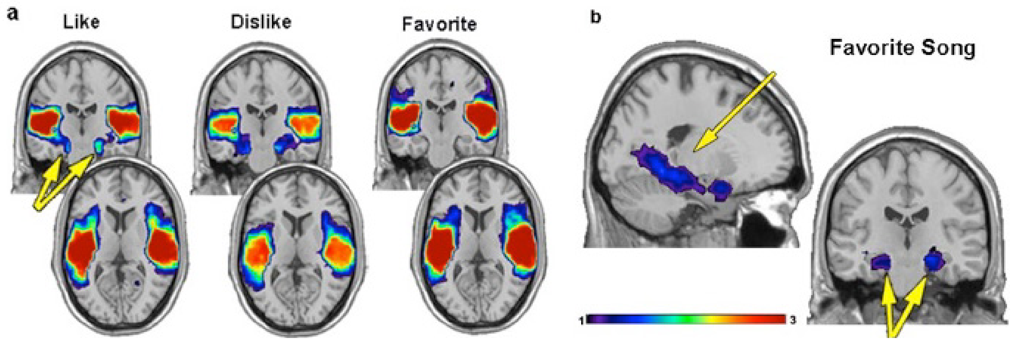


Figure 13. Demonstration of Differences in the Community Structure of the Hippocampus and Auditory Cortex When Listening to a Favorite Song. When listening to liked and disliked music, the hippocampi and auditory cortex were within the same community (a). The location of the hippocampi is indicated by the yellow arrows. When listening to a favorite song, the hippocampi were functionally separate from the auditory cortex and became an isolated community (b). Color indicates the consistency across subjects as assessed using scaled inclusivity (See Methods and Supporting Information

Discussion

The effects of music listening and preference on brain connectivity were investigated using network science techniques. To mimic as closely as possible a 'real-world' experience, complete songs rather than brief excerpts were used. The previous analysis indicated that specific genres affected the connectivity of the auditory cortex differently (Wilkins et al., 2012). This study set out to determine whether the application of network science techniques might reveal patterns of functional connectivity based on individual music listening preferences, including a pre-reported personal favorite song, regardless of the type of music (Wilkins et al., 2012).

Of particular interest to this study were brain mechanisms responsible for self-reflective thought and socio-emotional memory (Immordino-Yang et al., 2012; Raichle, 2010). Previous analyses with fMRI and naturalistic listening focused on brain network responses to specific components, such as timbral musical features and motifs, within a continuous musical excerpt (Alluri, Toiviainen, Jaaskelainen et al., 2012; Burunat et al., 2014). The results of this study revealed that when listening to complete songs, there were consistent patterns of network connectivity that exist within the brain that are related to preference. The findings revealed that liked, disliked, or favorite music dictates this functional connectivity, regardless of the type of music or the presence or absence of lyrics. The compatibility between these results and what music listeners frequently self-report in terms of neurobiology and neurorehabilitation are discussed below. Included re directions for future research based on the current findings.

The default mode or resting-state network has been shown to support specific brain functions, such as self-referential thoughts, emotional perspectives (i.e., empathy), and levels of self-awareness (Broyd et al., 2009; Gusnard et al., 2001). Described as functioning somewhat like a toggle switch between outwardly focused mind states and the internal or subjective sense of self, this network appears to include mind-wandering experiences such as imagining the future, the discovering of new possibilities (hopes), and the affective significance of aspirations or dreams (Immordino-Yang et al., 2012; Johnson et al., 2006; Raichle et al., 2001). The demonstrated high degree within the precuneus concurrent with high global efficiency provides preliminary support for the recruitment of other cognitive processing states when listening to music that is liked (Masataka & Perlovsky, 2012; Soto et al., 2009). Interestingly, these patterns were present regardless of the genre or lyrics. When listening to liked music, the consistency of the community structure within the default mode network suggests compatibility with the listener's experiences of musically-driven introspection (Juslin & Sloboda, 2001). This suggests that such connectivity might perhaps support neural processes associated with other aspects of cognition. Specifically, it appears that the default mode community structure results align with those self-referential or mind-wandering type experiences people report when listening to their preferred music (Gabrielsson & Bradbury, 2011; Rentfrow & Gosling, 2006).

The high degree of connectivity found within the precuneus combined with the default mode network community structure results suggest that listening to music that is preferred influences these emotionally laden experiences in the brain (Molnar-Szakacs & Heaton, 2012; Spreng & Grady, 2010). Research has revealed that disruptions and abnormal connectivity within the default mode network may be related to a set of neurological challenges, such as autism, mild cognitive impairment, post-traumatic stress disorder, schizophrenia, and depression (Assaf et al., 2010; Broyd et al., 2009; Jin et al., 2012). This network has also been more recently implicated in the development of cognitive abilities such as divergent thinking and creativity (Immordino-Yang et al., 2012; van den Heuvel et al., 2009). Based on these findings, it might be possible that listening to preferred music has the potential to engage such brain functions (Immordino-Yang et al., 2012). This has specific implications for neurologic remediation (therapy), where music has been shown to have neurorehabilitation effects, such as improvements in executive function and emotional adjustments, as well as lessening of anxiety and depression (Thaut, Demartin, & Sanes, 2008; Thaut et al., 2009). The results suggest that using each brain-injured person’s preferred music might have a stronger effect than disliked music. Along with the findings from Alluri, Toiviainen, Jaaskelainen et al.

(2012) who found a correlation of DMN activity with low-level timbral musical features, preferred music might better engage the DMN and thus affect the complex sensory-motor rhythmic integration that is observed with music neurorehabilitation.

Assessment of functional connectivity within the DMN, and particularly the precuneus, has emerged as a promising diagnostic measurement for patients suffering from disorders of consciousness (i.e., locked-in syndrome, vegetative state, and minimally conscious states) (Fransson & Marrelec, 2008; Owen, Schiff, & Laureys, 2009; Vanhaudenhuyse et al., 2010). Connectivity within the DMN has also emerged as a promising diagnostic measurement in autism (Cherkassky, Kana, Keller, & Just, 2006), where understanding the inner representation of other people's affective state (i.e., empathy) is often compromised (Molnar-Szakacs & Heaton, 2012). The results from this study suggest there may be some potential utility in listening to preferred music to optimally influence functional brain connectivity within this network (Fransson & Marrelec, 2008; Owen et al., 2009; Vanhaudenhuyse et al., 2010). Clearly, future research is needed to more fully understand how music listening impacts these brain mechanisms.

Research on the structure and function of resting state and task-based connectivity have focused almost exclusively on static representations of connectivity patterns (Bassett & Bullmore, 2006; Bassett & Bullmore, 2009). However, recent study results have indicated that functional brain networks are highly plastic can be altered spontaneously and by exogenous stimulation (Bassett et al., 2011). In conjunction with these findings, perhaps listening to music has the potential to alter brain network connectivity organization and that music preferences would dictate the connectivity that could be expected. While these results almost certainly have developmental and educational implications (Immordino-Yang, 2011), additional research needs to be performed in these areas.

Research evidence indicates that the hippocampus is critical in the formation of social and emotional memories (Immordino-Yang & Singh, 2011). The finding that the auditory cortex and hippocampus shared the same module when listening to liked and disliked music supports this implication. Recent results of Burunat et al. (2014) relate hippocampal connectivity with working memory for musical motifs during continuous listening. The results indicated that when listening to one’s favorite song, the hippocampus functionally separated from the auditory cortex. Perhaps, when listening to a personal favorite song the brain retrieves, rather than encodes, emotionally-laden autobiographic and episodic memories (Janata, 2009). This result is consistent with the notion that when listening to a favorite song or music, memory formation is no longer critical because memories associated with a personal favorite song have been previously encoded. In summation, by combining the two community structure findings, the results suggested that listening to a favorite song has the potential to not only recruit those previously encoded memories but also, even more importantly, to simultaneously support and sustain brain introspection via connectivity within the DMN, thus effectively re-processing autobiographic and episodic memories. Again, of interest was that this result occurred regardless of the type of music and the presence or absence of lyrics.

Combining the DMN and auditory/hippocampus findings, these results also suggest that listening to music that is Liked provides for the possibility of encoding new memories that are associated with prior self-referenced thoughts and memories. In contrast, when listening to the Favorite song, the encoding appeared as no longer necessary, and circuitry supporting self-referential thoughts within the DMN was dominant. This is in direct contrast to the Disliked condition when the hippocampus was still engaged with auditory cortex but the default mode network was disengaged. These findings may have implications for neurological challenges, such as autism, and neurodegenerative disorders, such as Alzheimer's disease (Assaf et al., 2010; Simmons-Stern, Budson, & Ally, 2010), as well as for human development and learning (Immordino-Yang et al., 2012). Clearly, optimal manipulation of the auditory-hippocampus network as well as the DMN could have important implications for complex neurological disorders and neurorehabilitation.

Summary

This study has shown that brain network connectivity patterns are associated with music listening and preference. The current findings indicated that regardless of the acoustical characteristic, functional brain connectivity states depended on whether the music is liked, disliked, or a favorite song. Listening to music that was liked or a favorite song affected functional connectivity in regions involved in self-referential thought and memory encoding, such as the default mode network and the hippocampus. While perhaps everyone intuitively understands the mental experience or feeling when listening to his or her preferred music, whether it is Beethoven's 9th Symphony or Eminem or when listening to one's favorite song, such as one from *Les Miserables* or Allison Kraus, the results from this study revealed that this similarity of experience was manifested in the brain by engaging the DMN. This was first study to apply network science methods to real-world music listening. The results provide a glimpse into the neural patterns underlying the emotion-cognitive states associated with listening to preferred and favorite music.

Methods

Participants

All methods were carried out in accordance with the approved guidelines from the Wake Forest University Medical Center Institutional Review Board. Participants were recruited by flyer and word of mouth and signed Informed Consent documents and experimental protocols approved by the Wake Forest Baptist Medical Center Institutional Review Board. Twenty-one young adults were recruited (average age 24 ± 3.4 yrs; 13 female) based on their most preferred musical genre: classical (n = 5), country (n = 5), rap/hip hop (n = 5), and rock music (n = 6). The genre-ranking of the 11 genres before enrollment in the study was used to ensure that there was not a bias toward participants who only liked a certain genre. All participants were right-handed, English speaking, color-sighted, had normal hearing, and were free from neurological disorders. Prior to scanning, participants completed a comprehensive questionnaire about formal musical training and a genre preference ranking of a total of eleven music genres (classical, country, gospel/blues, rap/hip hop, alternative, rock, Christian, folk, pop, metal, Broadway, jazz, classic rock). Prior to the scanning session, participants were asked to self-report a title of their most favorite song. Participants were instructed that their favorite song did not need to be specifically from their preferred music listening genre, merely that it was their favorite song. Participants provided the title of their favorite song to the experimenter prior to the scanning session. The favorite song was intentionally requested in order to analyze the functional brain connectivity responses separately from their preferred and non-preferred music.

The rationale for choosing to differentiate between overall preferred music and a favorite song was to determine if brain network responses might differ between the two. To clarify further, preferred music is a more broadly experienced musical listening phenomenon that can be envisioned as a preferred music listening overall experience, such as through on-line preferential music listening application streams such as Pandora or Groove Shark. On the other hand, and often in contradiction to one's overall musical listening preferences, an individual's all-time favorite song may not coincide with an individual's preferred genre. Indeed, in this study, there were many participants who reported a favorite song that was outside of their most preferred music listening genre. For example, one participant's preferred music was classical music but the self-reported favorite song was a country song by Garth Brooks, a country music singer and artist. Each participant's favorite song title and any other recording specifics, such as the specific artist, conductor, and/or year of performance was provided to the experimenter prior to the participant's scanning session. Ten subjects reported having formal musical training. Eight had completed, or were in the process of completing, a university music degree. Eleven reported that they could read music fluently. For the favorite song, participants were simply requested to self-report and provide a title to their favorite song by being asked , “I want the name of your favorite song, the one that, ‘Rocks your world’, ‘Floats your boat’, and ‘You love this song’”. Further details, including the pre-reported favorite songs, are provided in the supporting information of Chapter V.

Stimuli

Six musical selections, hereafter referred to as songs, were presented pseudo-randomly to each participant in the MRI scanner while blood oxygen level dependent (BOLD) functional MRI (fMRI) data were collected. The six songs, each five minutes long, included four pre-selected songs considered iconic within each musical genre, an unfamiliar selection, and a sixth personal favorite song. The five songs presented to every subject were Movement I from Symphony No. 5 by Beethoven (classical genre), “Water” by Brad Paisley (country genre), “OMG” by Usher (rap /hip hop genre), “Rock ‘N Roll All Nite” by KISS (rock genre), and “Spring Hall” by the Chinese Jinna Opera Band (unfamiliar genre). Favorite songs ranged from Rhinna & Eminem to Rachmaninov. For the complete list of favorite songs used in the study see Chapter V.

Scanning Procedures

Prior to the scan session, participants were trained to use a Visual Analog Scale (VAS) to rate how much they liked/disliked each song selection. With this procedure, we were able measure subjective preference across participants (Simmons-Stern et al., 2010). During the scanning procedure each participant listened to six musical selections. Each selection was presented as a continuous audio clip of five minutes with no interruptions. The music genre clips included rock, rap, classical, country, an unfamiliar piece, and their pre-reported favorite song. Before the onset of imaging and with the scanner on, participants had their headphones tested and the music volume adjusted. Prior to presentation of the musical selections, a five minute eyes-closed at-rest scan was acquired. During the entire musical portion of the scanning procedure, all participants had their eyes closed. Unbeknownst to the participants, songs were played for each participant in a randomized order based on an overarching scheme by genre preference from a pre-study music genre preference questionnaire. However, because the music preference questionnaire included rating scale choices of a total of eleven (11) genres, the 4 genre songs appeared as randomly presented to the participants. Each participant had previously provided the title of their self-reported favorite song that was presented last. Participants rated their preference for each song from 1-10 using the visual analog scale (VAS) when each selection ended and before the next song was presented. The highest VAS score report was used to determine their top preferred music during the scanning session. The lowest VAS score was used to determine their least preferred music during the session. The favorite song, the title of which was provided by each participant to the experimenter during the screening session, was presented last. See Chapter V for a discussion of possible ordering effects associated with the song presentation order.

MR scans were performed on a 1.5 T GE twin-speed LX scanner with birdcage 12-channel head coil (GE Medical Systems, Milwaukee, WI). For blood oxygenation level–dependent (BOLD) contrast, T2*- weighted functional images were acquired using a single-shot, gradient-recalled, echo-planar imaging sequence: TR/TE = 2000/40 ms, voxel size 3.75 x 3.75 x 5 mm^3. To allow for all songs to be played in their entirety, songs were edited for a total continuous playing time of five minutes. 150 brain volumes were collected per MRI run, and the first 6 volumes were not included in the network analyses, as this was the time during which the BOLD signal achieved steady-state.

Network Generation and Analysis

Network generation and analysis was performed using the fMRI time series data from each subject with eyes closed. Acquired images were motion corrected, spatially normalized to the MNI (Montreal Neurological Institute) space, and re-sliced to 4 x 4 x 5 mm3 voxel size with an in-house processing script using FSL package (FMRIB-University of Oxford). Imaging data was filtered (0.00945-0.084 Hz) and head motion (6 rigid-body transformation parameters) and mean signal (whole-brain, white matter, and ventricles) were regressed from the data to limit effects due to physiological noise (Fox et al., 2005; Hayasaka & Laurienti, 2010; van den Heuvel, Stam, Boersma, & Pol, 2008). Networks were then generated using a Pearson correlation with each voxel (~21,000) representing a network node. This produced a cross-correlation matrix containing the Pearson correlation coefficient representing the strength of association between each voxel pair.

The correlation matrix was then thresholded to generate a sparse network in keeping with other biological networks (Laurienti, Joyce, Telesford, Burdette, & Hayasaka, 2011). The threshold was based on a relationship between the number of nodes and the average node degree (K). This procedure ensured that comparisons across subjects were based on networks with comparable densities. Details of the thresholding procedure and the rationale for the chosen threshold are presented in the Supporting

Information. Briefly, the threshold is based on $S = \log(N)/\log(K)$. For the data presented here, a threshold of $S = 2.5$ was applied to the matrix, resulting in the binary adjacency matrix (A_{ij}). Once the complete adjacency matrix was generated for each subject, network statistics were calculated. The network statistics for each node were mapped back into 3D brain space to identify the spatial location of key network nodes and network communities. Networks were generated for each participant using the fMRI time series from each subject's six musical experiences. Results presented here are from the participants' favorite song and the highest and lowest rated songs from the five experimenter-selected genres. Therefore, three separate network calculations were conducted based on most and least preferred songs of the iconic music selections and one for their personal favorite song.

Network Properties

The analyses focused on four network properties: degree, global efficiency, local efficiency, and community structure. Degree (*K)* is the number of edges or *functional links* for an individual node. Global efficiency (Eglob) is a measure of the distance (in network space) from a given node to every other node in the network (Latora & Marchiori, 2001). Eglob is calculated as the average of the inverse of the shortest paths between node *i* and all other nodes in the network. This property is scaled ranging from 0 (indicating no path between nodes) to 1 (direct connection between nodes). Disparate regions of the brain can have high global efficiency if the path length for nodal communication is sufficiently short. Local efficiency (Eloc) is a measure of local neighborhood connectivity. Eloc is calculated by computing the global efficiency of a sub-graph of node i. In other words, it measures the distance between all the neighbors of node i. This statistic also ranges between 0-1, with larger values indicating that the neighbors of a particular node are highly connected to each other. A detailed description of the properties calculated in this study may be found in multiple review articles (Bullmore & Sporns, 2009; Fox et al., 2005; Rubinov & Sporns, 2010). Once network statistics were calculated, the location within the brain of the nodes with the highest statistics was evaluated. Visual depictions of network maps in brain space focused on “network hubs” heuristically defined as the top 20% of the nodes for each of the network statistics. Statistical analyses were performed by comparing the actual network statistics, with no arbitrary threshold, within specific regions-of-interest (ROIs) located in the precuneus and in the auditory cortex. The precuneus ROI was a 12 mm sphere centered at 0, -54, 34 in MNI space. The auditory ROI consisted of bilateral boxes (16 mm X 16 mm X 10 mm) centered at 54, -12, 2 and -52, -12, 2 in MNI space.

Community Structure

Community structure is a multivariate analysis that identifies collections of network nodes that are more interconnected with each other than they are with other network communities. The analysis used was based on modularity (Q) introduced by Newman and Girvan (2004). Details of the community structure analyses are presented in the Supporting Information. Briefly, hierarchical network partitioning was performed using the algorithm called QCut developed by Ruan and Zhang (2008). The optimal partition was identified using Q and was the basis of all further analyses. Due to the multivariate nature of community structure, it is not possible to simply identify a representative module for a group of individuals. However, scaled inclusivity (*SI)* is a statistic that can be used to determine the consistency of a given network community across individuals (Steen, Hayasaka, Joyce, & Laurienti, 2011). This analysis was used to evaluate the consistency of the community encompassing the precuneus and the community encompassing the auditory cortex under the three conditions (for detailed information see the supporting information in chapter V).

CHAPTER V

SUPPORTING INFORMATION FOR EXPERIMENT TWO

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The following supplemental manuscript was published in *Nature Scientific Reports* on August 28, 2014 and is reprinted here with permission. Stylistic variations and layout are due to requirements of the journal. However, the article has been modified from its original published version to create a consistent formatting style throughout the document for in-text citations and references. This supplemental manuscript includes supplemental methods and additional descriptions of network methods and data analysis.

Supporting Information

Supplemental Methods: Screening Session

Participants were asked to complete a comprehensive questionnaire during a screening session that was designed to eliminate any indication as to the intent of the study design prior to the scanning session. This screening session occurred several days to 2 weeks before the scanning session. The questionnaire included a Delphi survey of 26 exploratory questions about participants' ideas about music and their uses of music in their daily life. These questions ranged from such topic areas as whether participants use music to alter their mood to whether they enjoy mentally analyzing complex musical compositions. In addition, the participants were asked questions about their formal and/or informal musical training. The participants were asked to rank their personal preferences for eleven musical genres. The eleven musical genres included: rock, gospel, blues, rap/hip hop, jazz, classical, country, alternative (low-fi, experimental, punk, techno, mgmt, disco), metal, pop, and Broadway. The questions about participants formal years of musical training was defined by category: 0 years, 1-3 years, 4-7 years, 7-10 years and 10 plus years and a specific question about the musical instrument(s) the participant had received their formal or informal training on. This included their primary instrument as well as any secondary instruments (such as piano or guitar) and the number of years on each instrument. Participants were asked to estimate how much time they spend listening to music (average listening time was 3.4 hours per day). In addition, participants were asked whether they could speak or read a foreign language (French, Spanish, German or other) and were asked whether they could speak (or read) Chinese. Participants were also asked to rank their preferences for colors ranging from red to black (red, yellow, orange, blue, green, white, and black). Training was provided to participants on how to use the Visual Analog Scale (VAS) both in the screening session and just prior to the scanning session. Finally, each participant was asked to provide their most favorite song title and artist. In order to ensure that the favorite song was exactly what the participant requested, songs were carefully noted including artist, recording year, performing group and any other specific information that was needed. For example, one participant wanted the Prelude in D minor Op. 23 no. 3 by Sergy Rachmaninoff performed by Vladimir Ashkenazy. Participants were allowed—and even encouraged—to feel free to change what they considered their favorite song up until the day before the scanning session. This was done to ensure that the participants had been given ample time to determine what they would consider their favorite song. Many of the participants needed several days to determine what they considered to be their number one song, the one that ‘rocks their world’, ‘floats their boat’, and ‘is my favorite song’. No restrictions were given as to the genre (i.e. the type) of music or whether their favorite song should or should not have lyrics. Note that several participants had a favorite song that was outside of their preferred genre.

Additional MR Scanning Session Information

During the scanning session, all songs were presented to the participants without their prior knowledge of what music was to be played to them (apart from their favorite song). Thus, though they had reported a particular preference for a particular genre of music, all songs appeared to the participants as randomly presented. The songs are reported as being randomly presented because the songs were presented in an over-arching scheme that began with their preferred genre. However, given the enormous variety of choices for songs to present, that the participants did not know the music that they would be hearing (apart from their favorite song) and that the participants completed a questionnaire that highlighted 11 types of music to prioritize, it is the case that, at least from the participants’ perspective, the music was randomly presented. Thus, their brain responses were manifest from this perspective. Following the presentation of every song, each participant was asked to rate their preference for the song using the visual analog scale (VAS) as discussed in the Methods.

Table 2

Participants' Pre-Selected Favorite Songs

Favorite song	Artist(s)/composer
April 29th, 1992	Sublime
Come, Thou Fountain of Every Blessing	Mormon Tabernacle Choir
Das Verlassene Magdlein	Hugo Wolf
Days of Elijah	Robin Mark
A Better Son/Daughter	Rilo Kiley
Friends in Low Places	Garth Brooks
Gimme Shelter	The Rolling Stones
Breakeven	The Script
Human Nature	Michael Jackson
Love Like Crazy	Lee Brice
Love the Way You Lie	Rhianna & Eminem
Motorcycle Drive By	Third Eye Blind
Name	Goo Goo Dolls
Nessun Dorma from Turandot[a]	Puccini
Non Je ne Regrette Rien	Edith Piaf
One More Chance	The Notorious B.I.G
Symphony No. 2 in C minor[b]	Gustav Mahler
Rockin That Thang	The Dream
She	Harry Connick Jr.
Prelude in D Minor, Op. 23, No. 3[c]	Rachmaninov
You're Not Alone	Meredith Andrews

[a] Performed by Luciano Pavarotti

[b] Performed by The City of Birmingham Symphony Orchestra Conducted by Simon Rattle (requested the last 5 min. from Mvt IV)

[c] Performed by Vladimir Ashkenazy

Additional Description of Network Methodology

Threshold Determinations

Thresholds for Binarization of the Network. For the voxel-wise network, a Pearson's correlation coefficient was used to correlate the time series in each voxel. After creating the correlation matrix, a threshold was applied to yield a sparse matrix. There are researchers that suggest it is preferred to not threshold the networks and utilize a fully connected, weighted network (Rubinov & Sporns, 2011). However, it has been demonstrated that when connected networks are utilized in an information processing model, the networks do not exhibit behaviors expected from a small-world network (Joyce, Laurienti, & Hayasaka, 2012). In addition, fully connected networks must be much smaller (100s of nodes) than the networks that we use (~21,000 nodes) due to the computational complexity of the algorithms used to analyze the networks. The optimal solution to this issue remains equivocal and either method is currently valid. The use of sparse networks is preferred because it allows for higher resolution networks with many more nodes. The application of a threshold using the formula of $N = K^s$ has been shown to relate network size to density in random small-world networks (Watts & Strogatz, 1998). This threshold ensured that comparisons were made between networks of comparable density relative to the number of network nodes. For the networks used here, all subjects had approximately the same number of nodes so network size was not a limiting factor. For this study, a threshold $S = 2.5$ was used, so the relationship of $N = K^{2.5}$ was used. The choice of $S=2.5$ results in networks that exhibited comparable size: density ratios observed in other naturally occurring networks (Laurienti et al., 2011). In addition, results have demonstrated that networks tend to fragment when S is above 3.0 (Hayasaka & Laurienti, 2010), and the reproducibility of brain networks is highest at thresholds with S between 2 and 3 (Telesford et al., 2010). Once the threshold was applied, correlations above the threshold were given a value of 1, and those below the threshold were given a value of 0.

Definition of Network Hubs. The top 20% was used to generate representative images to allow visualization of the data. Based on the Pareto Law, the 20% choice is a heuristic. This is common in systems that exhibit power law or power law-like behavior. This cutoff is acknowledged as arbitrary but was used only for the visual depiction of the location of network hubs. In fact, there is, to date, no absolute definition of a hub. Recently, results have indicated that reproducibility of hubs within subjects across runs falls off dramatically above 20% and is relatively stable between 20 and 25% (Telesford, Laurienti, Friedman, Kraft, & Daunais, 2013). All comparisons across conditions used actual network statistics without applying this cutoff.

Determination of Community Structure

Module Determination. One can identify the community structure or modular organization of a network with modules or neighborhoods defined as groups of nodes that are more connected to each other than other groups of nodes (Newman, 2006). Modularity is currently considered the gold standard to define community structure whereby a modularity metric Q is calculated that describes optimal modular partition. Newman-Girvan developed modularity to define the resolution at which one looks at the community structure after hierarchical partitioning is performed (Newman & Girvan, 2004). Q identifies the partition that maximizes the within community links relative to the number of within community links in a random network. An algorithm called Qcut (Ruan & Zhang, 2008) was applied to break each participant's functional brain networks into the modules. The partition that mazimized Q was chosen for each run of Qcut. As with all community structure algorithms, Qcut potentially yields different solutions each time it is run. The Qcut statistic was applied to each subject's network 10 times for each condition. Over these 10 runs, it became clear which run(s) yielded the highest value for Q; in practice, the same modular structure with highest Q value would usually occur in many of the 10 runs, increasing confidence in the optimal result for modular organization. The run with the highest Q was selected as the representative modular partition for that subject.

Scaled Inclusivity. Comparing modular organization across individuals is difficult and an ongoing area of research. Scaled Inclusivity (SI) is a metric that makes it possible to evaluate the consistency of the community structure across different subjects with similar brain functional networks (Steen, Hayasaka, Joyce, & Laurienti, 2011). In brief, SI measures the overlap of modules across subject's networks. If modules exhibit disjunction, then the SI values are penalized. The equation for SI is

$$SI_V = \frac{|S_A \cap S_B|}{|S_A|} \frac{|S_A \cap S_B|}{|S_B|}$$

where SI_v represents the scaled inclusivity of a node V which is in module A in subject i and module B in subject j. S_A and S_B represent sets of nodes in modules A and B, respectively, and $\|$ denotes the cardinality of a set (Steen, Hayasaka, Joyce, &. Laurienti, 2011). An $SI_v = 1$ would indicate perfect overlap of modules from 2 different subjects. As the overlap decreases, the SI_v becomes less than 1. There are also penalties to the value of SI_v for different sizes of the modules as shown by increasing the denominator in the equation.

Si was calculated for all the community structure between all participants. In order to determine the consistency of any particular module, the individual with the highest SI values in the region of interest was identified. A subject-specific SI map was then created from a weighted sum of the maps comparing the subject's modules to all other subject's modules. This subject-specific SI map showed the consistency of a particular node falling within the same module across subjects. SI was the weight used in these weighted sums. In an ideal situation with all subjects having the exact same community structure, SI_v would = n-1 in every voxel. However, this is highly unlikely in biological data, so SI values are typically smaller than N-1. As part of this study, these SI modularity maps are the maps presented in Figures 11 and 13 of the main manuscript. For a more detailed description of SI, see Steen et al (Steen et al., 2011). Because the final SI calculations yield a single value in each voxel, there is no variance, and traditional hypothesis tests could not be utilized on this data.

Supplemental Results

Issue of Song Order

While there was no effect of song order on our results, presented here are all of the data about song order. Each participant's favorite song was presented last (6^{th}) after presenting the 5 pre-selected songs. These 5 pre-selected songs were presented for each participant in an order determined by how the participant ranked 11 genres of music at the screening session, which occurred several days or weeks before the MRI scan. The songs were chosen to be presented in an overarching scheme derived from the participant's most preferred genre to the least preferred, always ending with the unfamiliar Chinese opera (5th song presented). The song with the highest VAS score (i.e. most Liked song) was the first song for 8 participants, the second song for 8 participants, the third song for 2 participants, and the fourth song for 3 participants. The song with the lowest VAS score (i.e. most Disliked song) was the second song for 3 participants, third song for 4 participants, the fourth song for 3 participants, and the fifth song (unfamiliar, Chinese Jinna Opera Band for all participants) for 12 participants. The participants did not rank the musical selections. Rather, they simply used the VAS to show how much they liked the different songs (nothing was said about genres). 11 subjects reported a top "Like" VAS preference for the classical, 4 for the country, 3 for the rock, 3 for the rap, and 0 for the unfamiliar song. For the Dislike condition (subjects' lowest VAS score), 1 reported the classical, 2 reported the country, 3 reported the rock and 3 reported the rap song. 12 reported the unfamiliar music as their least preferred music.

Connectivity between the Precuneus and the Default Mode Network

A *post-hoc* analysis was performed to measure the connectivity between the precuneus and the remainder of the DMN. Figure S14 shows the ROI's used for the precuneus (an 12 mm radius sphere located at 0, -54, 34 in MNI space) and the DMN; these were derived from the work of Shirer, Ryali, Rykhlevskaia, Menon, & Greicius, (2012) as determined using independent components analysis. The red areas show the

DMN in its entirety. This image was kindly provided by Vinod Menon. The Cyan sphere shows the precuneus ROI used in this work. The green regions show the ROI that was used in this work to count connections from the precuneus ROI to the other portions of the DMN. The number of direct connections from the precuneus to voxels within the remaining DMN was minimal with the average ranging from 2 to 3 connections per voxel across the study conditions. The connections were measured one step further in the network. These were termed 2nd order connections. 2nd order connections are those connections that emanate from voxels directly connected to the precuneus ROI. Figure 15 shows the statistics for the number of 2nd order connections from precuneus ROI to the ROI located in the other portions of the DMN. These findings support the modularity findings showing differences in the precuneus module's connection to the rest of the DMN. The results revealed a significant (p = 0.04) increase in connectivity in the Like condition compared to the Dislike condition. There was no significant difference between Like and Favorite (p = 0.08) or between Dislike and Favorite (p = 0.71).

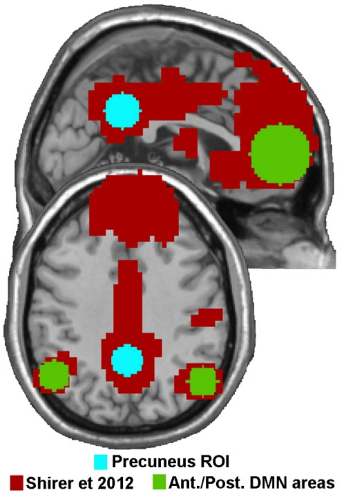

Figure 14. Depiction of Region-of-Interests Used in the Statistical Analyses.

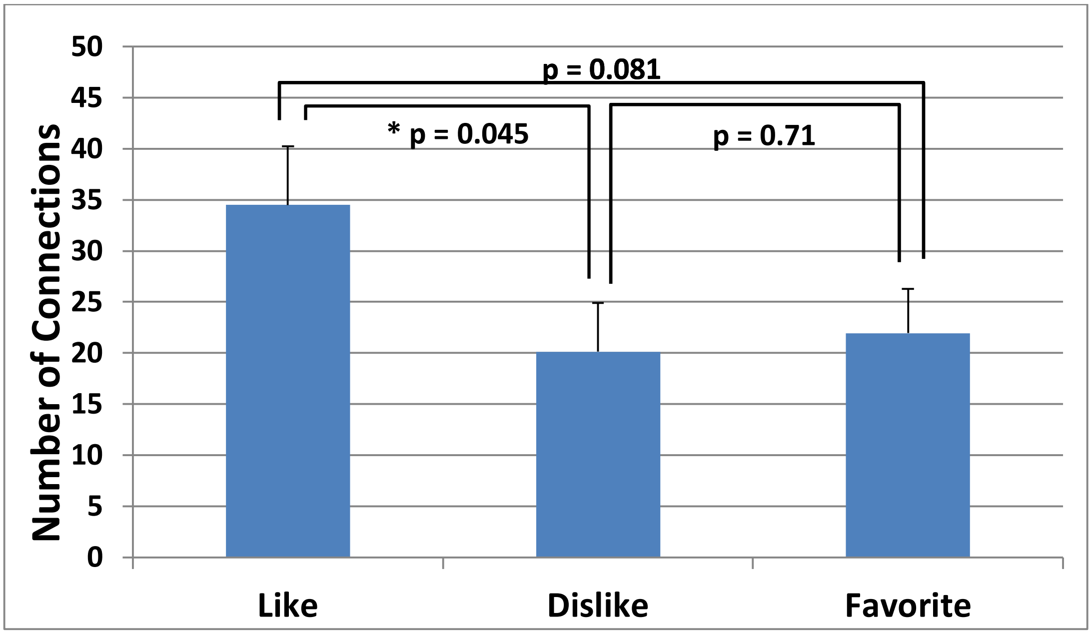

Figure 15. Average Number of 2nd Order Connections for Each Voxel between the Precuneus ROI and the ROI Located in the Anterior and Posterior Aspects of the Default Mode Network (DMN). There was a significantly greater number of 2nd order connections between the precuneus and the DMN ($p = 0.04$) in the Like condition compared to the Dislike condition.

CHAPTER VI

DISCUSSION AND IMPLICATIONS

The results presented in this dissertation suggest that listening to music plays a noteworthy role in the mental support and dynamic accessibility of self-related thoughts and memories. These mental activities appear to be important, formative, and life-sustaining phenomena. To begin this discussion, a few aspects about these results need to be mentioned. First, each of the findings needs to be conceptualized as a layer that provides increased understanding about how the brain responds to music. When the layered results are combined, the effects of music may be understood to be woven together as a blended collective or mental gestalt experience. In other words, the combination of results or findings demonstrates the composite picture or landscape that transpires in the brain during a continuous music listening experience. Second, results of the experiments, included in this dissertation, include responses subjected to technical limitations of fMRI. Finally, the series of studies in this dissertation are exploratory in nature. The results are the direct outcome of the new tools and techniques from the field of network science and a complex systems approach to understanding the brain. The implications of these results for education and clinical health practitioners are discussed in this chapter. Specific attention is given to how the phenomenon of musical enjoyment may affect learning and development (i.e., neurodevelopment) as well as neurorehabilitation (i.e., therapy). Future network science research with music, however, may provide a more complete understanding of the effects of music on the brain.

Specific discussion topics related to the evidence from these studies include:

- Default Mode Network and Preferential Music
- Musical Preferences: Educational Influence
- Music and Global Efficiency: Implications for Higher-Order Functions
- Auditory Descrimination and Music: Implications for Speech and Language Comprehension
- Children's Learning and Preferred Music
- Further Implications for Human Growth and Development: Favorite Songs
- Memory and Music: Adults, Dementia and Levels of Awareness
- Preferred Music and Behavioral Outcomes
- Theoretical Implications: Emotional Responses to Music
- Final Thoughts: Special Implications for Music Education Practitioners

Default Mode Network and Preferential Music

Listening to music that is preferred appears to spontaneously trigger brain circuits within the default mode network (DMN), and thus, engage the brain in mental processes that sustain the rumination of personal thoughts and memories. This network is implicated in mind-wandering, self-referential thoughts, emotional perspective taking (e.g., empathy), the discovery of new possibilities (e.g., hopes), and the affective significance of aspirations or dreams. As self-referential states, these mental activities are considered important to both human growth and development.

As previously discussed in Chapter IV, the DMN is described as functioning somewhat like a toggle switch or revolving door between the internal mental representations of the self and outwardly-focused mind states. This network appears to align with how people typically describe their mental life. The mind gently bounces around, subtly moving back and forth between externally focused mind states and the subjective sense of self. The effects of preferred music listening appear to influence this process. The consistency of the community structure evidence suggests compatibility with persons' self-reported experiences of spontaneous thoughts when listening to their preferred music. The high degree within the precuneus, in conjunction with the entire default mode network community structure, suggests that musically triggered self-reflection is possible. The DMN appears to be aligned with specific mental states that are important in human cognition. The DMN functional connectivity results appear to support those unsolicited, self-referential, or mind-wandering type experiences that people frequently report when listening to their preferred music.

As reviewed in Chapter IV, connectivity disruptions within the Default Mode Network are implicated in a host of cognitive problems and a wide variety of psychological diseases and mental disorders. Recent research has revealed that functional brain networks are highly plastic and can be altered spontaneously by exogenous stimulation (Bassett et al., 2011). Emerging evidence has indicated that compromised connectivity and disruptions within the DMN are related to a host of neurological challenges such as autism, mild cognitive impairment, depression and post-traumatic stress disorder (Broyd et al., 2009).

The results of this series of studies suggest that preferred music has specific implications to influence and potentially to remediate these mental states. Again, listening to preferred music might help toward remediating these disorders in the brain (Wan & Schlaug, 2010). The implications of the evidence, however, extend beyond the more disruptive neurological problems. Perhaps preferred music listening is useful to mind wandering experiences that support a healthy internal mental life (Altenmüller et al., 2012). Perhaps listening to preferred music supports reflective states related to maintaining well being and mental equilibrium. This idea would align with emerging results suggesting that listening to music helps resolve mental stress (i.e., cognitive dissonance) in adults and children (Khalfa, Dalla Bella, Roy, Lupien, & Peretz, 2002; Khalfa, Dalla Bella, Roy, Peretz, & Lupien, 2003; Masataka & Perlovsky, 2012). Certainly, additional research is needed to fully understand these brain mechanisms, but recent evidence combined with the results presented in this manuscript suggests this type of spontaneous alteration of brain networks during music listening is possible.

The DMN also has been implicated in other cognitive processes such as mind-wandering activities related to imagination and creativity (i.e., making new connections between previously disparate information as original thoughts or useful ideas) (van den Heuvel et al., 2009). Music preference alters the brain network in this interconnected region. The results suggest that listening to preferred music influences default mode network processes. In contrast, the results from the present study suggest that listening to disliked music does not engage the default mode network.

Listening to preferred music also functionally connects pivotal regions within the DMN to frontal regions of the brain though global efficiency. Frontal regions are implicated in executive functioning processes such as decision-making and working memory. When listening to preferred music, the global efficiency from pivotal regions within the DMN (i.e., the precuneus) to frontal regions suggests that the mind can listen to music while simultaneously working on a problem at hand. This finding aligns with individuals' experiences of listening to preferred music while working or studying (e.g., minimizing mental distraction and increasing the ability to focus attention). If the results of these studies are conceptualized into a cohesive whole, the implications from the study of effects of music on functional connectivity suggest that listening to preferred music coordinates between emotionally influenced default mode states and outwardly focused mind states useful for other cognitive processes. Although subtle, these two effects appear to be very compatible with what people typically report when listening to preferred music. People often work, drive, study or perform other activities (e.g., jogging or exercise) while listening to music they enjoy.

Musical Preferences: Educational Influence

Ethnomusicologists have provided ample evidence that musical preferences are intimately tied to teaching and training (Fast & Pegley, 2012). For shaping and cultivating music preferences, thus, there is no blank slate. Whereas biological research evidence suggests preference for consonant over dissonant music (Trehub, 2003), the research was completed with traditionally Western chords. Evolutionary biological and anthropological evidence, however, suggests that people change, modify, and adapt (i.e., enculturate) musical tastes across time (Juslin & Vastfjall, 2008; Muller, Hofel, Brattico, & Jacobsen, 2010). Indeed, Western musical compositions clearly have changed across time (i.e., from Baroque with predominantly harmonic structures to the highly dissonant 12-tone music of Schoenberg and beyond). Stated simply, genres, songs, and different styles of cultural and historical music are widely diverse. One could speculate that developing enjoyable experiences with particular styles of music during growth and development will have an impact on potential DMN connectivity.

For music educators, music preferences may be cultivated or shaped, and thereby, are a powerful component of influence on an individual's overall development. The choices in musical selections ultimately may mold listening preferences and subsequently directly impact internally focused mind states via the DMN when listening to music. The results presented in this document suggest that enculturation of the brain through music may be an avenue for influencing social behaviors. An underexplored phenomenon that is currently not well understood, social and behavioral evidence suggests preferred music has influence on, or 'power' over, human behaviors. These musically influenced behavioral phenomena carry specific implications for the molding of musical preferences. Preferred music might be used as a cultural tool; music that either promotes behaviors of compliance and stability or persuades behavioral upheaval (e.g., cultural or religiously). Future research might clarify the possibility of whether preferred music is an influential change-agent, and whether specific socio-behavioral outcomes might be anticipated or may occur based on the influence of shaping preferred and disliked music.

Educational practitioners who select music for children perhaps should consider these results carefully. An implication of the preferred music phenomenon, as related to brain behaviors, is that the music, which children learn to enjoy, influences specific mental activities in the brain during development. The DMN connectivity suggests that listening to preferred music influences emotionally laden connections in the brain. The potential neurological influence of music appears to contribute to the template of a young mind, particularly because development is not stable until later adulthood. Results from this study reveal that this effect is in place regardless of the presence or absence of lyrics.

Emotional responses to music appear to help define the phenomenon of music preferences and enjoyment. For educators, emotionally satisfying music (i.e., preferred music) has specific implications. Neurobiological and neuroscientific evidence suggests that all learning, attention, memory, decision-making and social functioning are profoundly affected by, and deeply subsumed within, the process of emotion and aspects of emotional thought (Damasio, 1994; Darwin, 1979; Immordino-Yang, 2011; Immordino-Yang, Christodoulou, & Singh, 2012). To this end, the implications of these results are that experiences with preferred music might spontaneously support these educationally important mental processes for learning. The functional connectivity within the community structure of the DMN is present regardless of the presence or absence of lyrics. To underestimate the emotional influence that listening to music might have during development may be unwise. The music a young adult enjoys appears to be a phenomenon that alters brain connectivity. Future research with specific lyrics blended with preferred music might reveal whether similar self-reflective mind wandering activities influence similar patterns of connectivity.

Music Preferences and Global Efficiency: Implications for Future Research

Research-based evidence from the studies within this dissertation also has revealed that listening to preferred music increases global efficiency to frontal regions of the brain. Perhaps listening to preferred music influences the mental ability to perform other emotionally-driven cognitive functions (eg., attention, memory, decision making, and social functioning). Future research needs to be conducted to fully explore these results. Listening to preferential music has been reported to affect cognitive outcomes beneficial to mental function and recovery (Sarkamo et al., 2008). Stated generally, the results suggest future research is needed to fully understand the effects of music listening on mental states that, in turn, influence potential social behaviors.

Auditory Development and Music: Implications for Speech and Language Comprehension

Listening to classical music generates a high degree of connectivity within auditory regions (i.e., the auditory cortex) of the brain. The results of Experiment One, presented in Chapter III, reveal that listening to classical music generates high degree hubs of connectivity within the auditory regions. The auditory cortex is necessary for hearing, speech, and language comprehension. The implications of this result suggest that training for listening to complex musical compositions may provide an opportunity for the auditory cortex to develop responses to complex harmonic and melodic sequences (Koelsch, Schroger, & Tervaniemi, 1999). This conclusion has specific implications for speech and language comprehension that may result from listening to harmonically and rhythmically complex (i.e. classical) music. Kraus et al. have demonstrated that children who undergo intensive musical training appear to experience improvements in speech and language perception (Anderson & Kraus, 2011; Kraus & Chandrasekaran, 2010; Kraus et al., 2014; Musacchia, Sams, Skoe, & Kraus, 2007; Slater, Tierney, & Kraus, 2013). The type of intensive musical training was specific to Western (i.e., classical) music. Future research needs to be conducted to determine whether non-Western musical training has similar effects. Understanding and decoding someone's affective state is often conveyed through the delivery (i.e., the prosody) of the voice (Overy & Molnar-Szakacs, 2009; Quintin, Bhatara, Poissant, Fombonne, & Levitin) in conjunction with facial expressions. Musicians performing musical compositions deliver a host of finely coordinated auditory stimuli. Highly complex musical compositions contain melodic and harmonic motifs and phrases blended with dynamic sets of interacting frequencies, waveforms, and intensities.

Perhaps exposure to music during developmental years is helpful to pitch discrimination and the acoustical decoding of speech and language processes, particularly prosody delivery (Overy & Molnar-Szakacs, 2009; Sander et al., 2005; Tierney, Krizman, Skoe, Johnston, & Kraus, 2013). An accurate understanding from the prosody of speech has particular implications for neurological challenges such as autism, where the comprehension of another's emotional state (i.e., empathy) is often compromised (Molnar-Szakacs et al., 2009). The emotional message in speech, is delivered through prosody and tends to contain the feelings or intentions of the speaker. Some research evidence has suggested that musical training can help with dyslexia, where mental disruptions in synchrony and timing deficits appear to influence written language comprehension (Overy, 2003; Overy, Nicolson, Fawcett, & Clarke, 2003). Although still underexplored, researchers offer that this suggestion may be the case (Gaab, Gaser, Zaehle, Jancke, & Schlaug, 2003; Strait & Kraus, 2011). The implications, however, also apply to other language-based pro-social behaviors, such as the ability to socially 'tune in' and emotionally and empathetically respond, or socially interact (i.e., get along well), with others (Painter & Koelsch, 2011). These 'pro-social' abilities are considered important for success in school, the workplace, interpersonal relationships, and society. Further research needs to be performed to understand fully whether an emotional understanding of speech prosody, as an empathetic response, is more successfully influenced through musical training, but the results hint that this is possible (Molnar-Szakacs & Overy, 2006; Overy & Molnar-Szakacs, 2009).

Children's Learning and Preferred Music

Enjoyable music is often a fundamental component of children's learning. Songs that contain learning lyrics, including basic hand-to-eye coordination songs such as "Itsy Bitsy Spider", are often considered successful tools in education. The results of the findings reported in this dissertation, concerning auditory-hippocampus community structure, suggest that preferred music is encoded, along with social and emotional memories, into long-term memory for consolidation. As a brain-based phenomena, the idea that preferred music changes the brain network has specific implications for educational practitioners. Listening to a favorite song changes connections of the community structure between auditory areas and the hippocampus, a region known for memory encoding and consolidation. The hippocampus is recognized for encoding socially and emotionally laden autobiographical memories. The evidence, presented in this dissertation, therefore, suggests that emotionally preferred music facilitates the encoding of socially and emotionally laden autobiographical memories for later retrieval. Additional implications, associated with the studies of this dissertation, are that listening to a favorite song functionally changes connectivity within the hippocampus and helps to facilitate successful retrieval of social and autobiographical memories. Favorite music is clearly preferred; therefore, functional connectivity within the DMN will be triggered. The results blend as a collective effort; thus, thoughts and memories related to the favorite music facilitate successful retrieval of information to be experienced again, and consequently, reprocessed.

The results of listening to disliked music and auditory-hippocampal community reveal that listening to music that is disliked will also encode memories. In contrast to favorite music, however, the disengagement of the hippocampus from the auditory cortex combined with the absence of connectivity within the DMN community suggests that the previously encoded memories will not support the self-referential mind-wandering states useful to desired mental health.

Finally, music is often a component of children's television programming and movies. The results of the present studies suggest that the type of music a child prefers, in turn, is mapped onto cognitive, emotional, and social developmental processes. Preferential music includes the music used for highly successful television and film programming with positive themes. Thus, a song such as “When You Wish Upon a Star” acquires new meaning for the listener, at least in terms of the listener's functioning brain. For example, envision a music classroom filled with children, a pre-teen listening to music on an iPod or an adult listening to an online preferred-music application platform such as Pandora or Grooveshark. Preferred-music supports the mental reprocessing of encoded thoughts, as well as activates useful mental resources in attention or working memory (i.e., holding something in mind). The auditory-hippocampal community encodes autobiographical emotionally laden memories during listening to music that is strongly preferred. If the music becomes a personal favorite, the previously encoded autobiographical memories within the hippocampus is dominant. Evidence has suggested that if the song is not preferred, or is distinctly disliked, the opposite effect occurs.

Educational practitioners should keep in mind that memories associated with favorite songs may be accessed via the hippocampus and DMN connectivity for a very long time. Future research is needed to verify this implication, but the results suggested that this connectivity in the brain is possible. This would likely include teaching songs such as “ABCs”, “Itsy Bitsy Spider” and educational jingles such as “Conjunction Function*”* and “Hypotenuse Triangle”, or other songs from School House Rock (Ovetz. 2011), or similar children’s television programming. Additionally, autobiographical memories previously encoded to favorite songs are accessible. The evidence, presented in this dissertation, includes functional connectivity analyses on fMRI data collected while participants listened to their self-reported favorite songs that included a variety of genres and lyrics. The hippocampus connectivity findings suggest that listening to a favorite song appears to be a previously encoded memorable experience with emotionally tagged moments. For example, an older person who saw the movie, "Casablanca," years ago can envision the musically triggered memories depicted in the movie. Indeed, it is remarkable how stable memories are when listening to favorite music or songs (Janata, Tomic, & Rakowski, 2007; Sherratt, Thornton, & Hatton, 2004; Simmons-Stern et al., 2010). Previous research and the current studies suggest that listening to a favorite song will spontaneously trigger the emotionally-laden personal memories that previously have been encoded by the hippocampus (Simmons-Stern et al., 2010).

Further Implications for Human Growth and Development: Favorite Songs

The effects of listening to favorite music have particular implications for understanding the influence of music on young adults during adolescence. Technological advancements have made music easily accessible, nearly commercially free, and overwhelmingly abundant. For example, a recent Google search indicated that young people, between the ages 12-17 years, spend an average of 2.5 hours per day listening to music. The poorly understood phenomena of emotional responses to music contributes to a fundamental lack of understanding of the role that music plays during human development. Numerous individuals report that their emotional-mental states are often more fully expressed through music than other media (e.g., words or language). In light of these opinions, perhaps future research on the effects of preferred music might reveal how mental-emotional states are mediated and transpire during development. A full understanding of how music affects cognitive–emotional response systems may advance our knowledge of other mechanisms that contribute to complex developmental states and behavioral outcomes during teenage years.

Historically within neuroscience, emotions have been out of reach empirically. Perhaps listening to music is useful during adolescence—a particular time of emotional challenge and upheaval—for mentally deconstructing or mediating complex cognitive–emotional responses to autobiographical experiences. An increased understanding of this musically-driven phenomenon may also provide insight into other emotional-response brain challenges that are currently not well understood (e.g., stress, anxiety, depression, ADHD and PTSD). These challenges often result in debilitating human motivational-response behavioral systems. The results reported in this dissertation suggest that listening to preferred music might help to alleviate or reduce these undesirable behavioral states and responses. Although poorly understood neurologically, perhaps the use of enjoyable or pleasurable music may provide a tool to understand how these brain-behaviors, as states, occur. Additional research is needed, but perhaps preferred music provides exogenous brain network remediation that is a non-invasive alternative to pharmacological interventions, and thereby, help to alleviate or reduce depression, stress and distress (i.e., emotional 'pain') (Koelsch, 2009).

Memory and Music: Adults, Dementia and Levels of Awareness

The evidence presented in the studies of this dissertation suggests that there are clinical applications for preferred and favorite music. Emotional responses to music (i.e., preferred music) appear to have a positive affect on patients with memory disorders (Samson, Dellacherie, & Platel, 2009). Listening to a favorite song suggests that the brain will access long-term memory systems related to autobiographical memory (Simmons-Stern et al., 2010). The connectivity within the hippocampal community structure during favorite music listening has special implications in neurodegenerative diseases where memory is often compromised, such as Alzheimer's disease. Being able to access memories via music has specific implications for memory caregivers and clinical health providers for potential neurological therapy (Sacks, 2007). Perhaps simply playing a favorite song temporarily may encourage emotional responses and remediate mental fragmentation and the loss of self-related thoughts. This would be a comforting and helpful outcome of preferred-music listening for those suffering from memory loss.

Preferred-music listening also has implications for other forms of dementia and compromised levels of mental awareness. Assessment within the default mode network has been suggested to provide a promising diagnostic measurement for patients suffering from disorders of consciousness (i.e., locked-in syndrome, vegetative state, and coma) (Owen et al., 2009; Schiff & Fins, 2007). In the present studies, results have revealed that preferred music triggers a high degree of connectivity within pivotal regions of the default mode network and changes the default mode network community structure. Based on this evidence, perhaps preferred and favorite music provides an evidence-based tool to further investigate, diagnose, or improve compromised levels of awareness from stroke or traumatic brain injury. Though still anecdotal, the 2014 documentary *Alive Inside!* suggests that listening to favorite music facilitates a person's transition from being non-respsonsive to being more fully aware of him- or herself. The evidence from this dissertations provides a scientific measurement to know whether persons in a non-responsive state have the potential to recuperate long enough to become aware of themselves and their outside world (musicandmemory.org; https://www.aliveinside.us). This resulting evidence would offer a non-invasive means to provide a potential baseline to encourage intervention and recovery measures (Sacks, 1983). Future research is needed, but the results suggest this neurological remediation through music might be possible.

Preferred Music and Behavioral Outcomes

History appears to provide ample evidence that music is a component of cultural-political ideological change resulting in different social behavioral outcomes (Berman, 2001; Hargreaves & North; Hodges & Sebald, 2011). The outpouring of the dissent music of the 1960s during the Vietnam War, music during the Civil Rights Movement, and Wagner music during WWII Germany (Fast and Pegley, 2012) are but a few examples of how preferred music can wield powerful changes in behaviors. Stated in a general sense, the effects of preferred music appear to contribute to mental states that, in turn, influence behaviors. Results within this dissertation have revealed that similar brain-pattern responses are present regardless of the presence or absence of lyrics. Implications of preferred music with lyrics for changing or sustaining themes of socio-cultural behaviors might be influential, particularly since preferred music is connecting the community structure of default mode network to frontal regions within the brain.

Theoretical Implications: Emotional Responses to Music

The introspective state (e.g., what the mind feels, remembers, or envisions) appears to connect subtle systems that form a sense of personal identity. Results from studies of this dissertation suggest that each person has these mental experiences that emerge from within the brain when listening to music and that these states are important life-sustaining phenomena and are crucial to a sense of self. Music is used as a means of engagement in almost all of life's activities. Whether tangentially listening, passively absorbing a soundtrack while watching a video or film, or actively attending a musical performance, people use music as a means to mediate between themselves and their external worlds. Indeed, music is such an integral part of life that it is difficult to imagine a world without music.

As previously stated, one of the more compelling features of music is that individuals primarily listen to music because of how it makes them feel. Additionally, individuals often report having very distinct, often unsolicited thoughts and emotionally laden memories when listening to strongly preferred music. Theoretically, the evidence presented from the current studies suggests that listening to music, as a music-to-mind process, supports a sense of individuality. The mind is filled with endless twists and turns wrapped into countless moments that emerge as a cohesive whole to create something new; the blended awareness of an individual self. The human mind cannot be reduced to simple, concrete, or discrete brain states. Individuals need to fluctuate, roam, and wander within their minds. These actions help individuals identify themselves as uniquely human. The results presented within this dissertation suggest that music may provide a mechanism for supporting these subtle and important processes in the brain.

The evidence of the studies included within this dissertation theoretically suggest that perhaps music provides a mechanism to sustain and mediate levels of self-awareness (i.e., by sustaining personal thoughts and memories), and thus, provide a sense of individuality. People are complex beings; they feel, move, remember and imagine. A loss of memory, a fading of the self, or being non-responsive is tragic. Unraveling why listening to a piece of music might connect the same brain systems in people (e.g., between the hippocampus and DMN) has opened up an avenue for scientists to pursue how other internally-focused thoughts and memories transpire in the brain that are unique to individuals yet common across all people. How the mind generates individualized awareness (i.e., consciousness) is currently an emerging frontier in neuroscientific research. Results of the current studies suggest that music may play a supporting role in the formation of these processes and provide a useful framework for understanding them within the brain.

Final Thoughts: Special Implications for Music Researchers and Education Practitioners

For music researchers and practitioners in music education, understanding that musical experiences appear to align with brain networks, associated with self-referential thoughts and memories, has unique implications. First, that music usually is experienced at very early ages (e.g., as an infant) supports the premise that musical experiences are naturally folded into the mental-developmental process for very young children. Continuing music experiences may provide a fundamental platform or foundation for normal adolescent growth and development. Second, generating experiences that are structured around shaping musical preferences may hold promise for particular socially driven behavioral outcomes.

Finally, a music teacher may find it beneficial to consider that enjoyable songs and preferred music are influencing the same brain systems that are subsumed into long-term memory processes. Another implication of the results from the current studies are that disliked music also may alter fundamental mechanisms in the brain. Listening to preferred music alters functional brain networks that assist and support important mental states. In summary, the results suggest that musical preferences and listening to music affect functional brain networks that are fundamentally important across a human being's life span.

Summary

The present understanding of the effects of music on the brain is merely in its infancy. Network science provides promising methods to uncover how other musical experiences, including musical training, may affect the brain. Fundamentally, thoughts and memories blended with emotionally laden experiences help individuals know that they exist, influence how individuals understand themselves, and affect how they interact with and understand others persons in the world. Listening to music provides a unique neuroscientific opportunity for understanding these experiences in the brain.

Emerging neuroscientific endeavors and clinical challenges require an understanding and accounting for how the brain manages to merge thinking and feeling. The need for a neuroscientific understanding of emotionally-influenced mental states encompasses artificial intelligent systems, machine learning, human development, recovering health, sustained well-being and successful aging (Tamietto & de Gelder, 2010). Through a network science approach, a full understanding of how music alters brain connectivity provides an unprecedented avenue to pursue fundamental questions about the human mind. The vast system of brain complexity, as a finely coordinated system, is nested within a mass of tissue floating inside the compartment of a skull. Understanding how the brain gives rise to a mind with emergent properties, such as conscious awareness and a sense of individuality is one of the grand challenges of the 21st Century. This quest for understanding how the thinking mind is simultaneously dwelling and intertwined with complex emotions is crucial for scientists to advance the understanding of the human brain. This series of exploratory studies, reported in this dissertation, reveals that a network science approach holds unique promise for helping discover answers to longstanding neurobiological and evolutionary questions related to the effects of music on the human brain.

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APPENDIX A

GLOSSARY

Adjacency Matrix: A graph can be represented as a network in a matrix format. The adjacency matrix is also referred to as the connectivity matrix. The adjacency matrix is configured based on the presence or absence of a connection between two node (i.e., node pairs). The brain adjacency is determined based on the thresholding procedure applied. This is currently an active area of research. For comparisions of brain networks across people, the research indicates that thresholds of 2.5 to 3.0 are considered statistically sufficiently robust. A more thorough review of thresholding procedures for brain networks may be found in Hayaska and Laurienti (2010).

Assortativity: The assortativity coefficient is a correlation coefficient between the degrees of all nodes on two opposite ends of a link. A positive assortativity coefficient indicates that nodes tend to link to other nodes with the same or similar degree.

BOLD: Blood-Oxygen-Level-Dependant is a signal measured in fMRI. In brief, when neurons become highly active they require glucose which must first be delivered by blood. As newly oxygenated glucose infused blood flows toward an area of the brain and the BOLD signal increases. It is actually a measurement of oxygen-extraction fraction of the BOLD signal with fMRI (i.e., the hemodynamic response function) but it is sufficient to understand that the BOLD signal increases when the neurons are more active. When a subject is performing a task, areas with high BOLD signal have more active neurons—which may indicate that those brain regions are responsible for the neuronal processes underlying that particular task. Thus, the BOLD signal is actually an indirect measurement of underlying brain activity.

Centrality: Overall, centrality measures how influential a node is within a particular network. There are several different measures of centrality and each may be applied to the adjacency matrix. The degree of a node is typically the first indicator of node centrality in the network. Centrality measures the number of connections a node has via short paths to other nodes within the network. Typically, high degree nodes are hubs and therefore exhibit high ‘betweeness’ centrality. For a further explanation of various centrality metrics see Joyce et al. (2010).

Clustering Coefficient: The clustering coefficient is the fraction of triangles around a node and is equivalent to the fraction of a node’s neighbors that are also neighbors of each other.

Community Structure: The community structure is the topological configuration across the network measuring nodes that share more inner connections than outer connections to other nodes in other modules. The optimal community structure is a subdivision of the network into non-overlapping groups of nodes (i.e., modules) in a way that maximizes the number of within-group edges and minimizes the number of between-group edges. The modularity statistic quantifies the degree to which the network may be subdivided into such clearly delineated groups. Similar to the concept of defining neighborhoods, communities can be defined by different partitioning measurements. For brain networks, community structure analysis is currently a highly active area of research. Finding and evaluating community structure in networks is presently based on the work of Newman and Grivan, 2004 and uses the Qcut algorithm developed by Ruan and Zhang, 2008. To determine sufficiently robust module partitioning, there are several ways to determine the network comparison and overlap of nodes across groups of participants including Scaled Inclusivity (SI). For a review, see Steen et al., (2011).

Connectivity: Connectivity specifically refers to the patterns of connections that are found among nodes in the structural or functional network.

Complex System: Complex systems are heterogeneous, self-organizing and strongly interactive. A complex system behaves quite differently from what we would expect by simply adding up activity or summing pairs of interactions. Self-organizing systems are not additive; they're emergent and display behaviors that have emergent phenomena. This is precisely why some of the collective behaviors cannot be predicted in advance.

Correlation Matrix: A correlation matrix describes the strength of connections between every pair of nodes in the network. The correlation matrix is generated by calculating the cross-correlation (i.e., pearson product moment correlation statistic) in the fMRI time series data between each pair of nodes. Positive values close to +1 indicate a strong positive correlation between two nodes, which negative values indicate close to -1, which indicates a strong negative correlation between two nodes.

Cortical Thickness: Cortical thickness is a morphological measurement that describes the thickness of the layers of the cerebral cortex of the brain. Cortical thickness roughly correlates with the number of neurons within the column of the cortex layers and is usually measured from the local or average distance between the white matter surface and the pial surface.

Degree: The number of inner and outer connections of a node, often referred to by the symbol (*K*). Throughout the entire network, node degrees can be summarized into a degree distribution. If a node has a total of 7 edges or links to other nodes in the network it would be said to have a degree of 7 or *K*=7.

Default Mode Network: An interconnected set of regions in the brain that appear during fMRI data acquisition when the brain is active but at rest.

Degree Distribution: The degree values of all nodes in a network may be used to form a distribution. The distribution in brain networks are often complex and are therefore not normally distributed and considered as following an exponentially truncated power-law. This type of distribution means that the majority of the nodes have fairly low degrees—or a lot of low degree connections—while a minority (i.e., a few) nodes have extremely high degree connections.

Efficiency: Efficiency is an inverse measurement of path length. Shorter path lengths imply a more rapid transfer between nodes in the network. Nodes with short path lengths do not necessarily mean they are connected by regional proximity. Akin to communication cell phones, nodes with efficiency may be far apart but are able to communicate rapidly and thus, ‘efficiently’ regardless of location.

Electroencephalography: Electroencephalography (EEG) measures electrical signaling within the brain and is temporally robust, on the order of milliseconds. Spatially, EEG is able to measure rapid electrical firing of neuronal signaling, but, is not able to capture and measure regional specificity nor uncover activity location(s) deep within the brain.

Functional Magnetic Resonance Imaging (fMRI): fMRI is a brain imaging technique that is based on the precession of the magnetic moment of nuclei within the nucleus of the neuron.

Global Efficiency (Eglob): The global efficiency is the measurement of distant information transfer in the brain. It is inversely related to path length. A node with high global efficiency tends to be connection to many regions of the network. Globally efficient nodes are nodes that are regionally separated from other nodes in the network but are still connected, via short path length, regardless of their location within the network. Thus, globally efficient nodes share 'close contact' and are thought to be able to communicate rapidly between each other regardless of their location.

Gray Matter Volume: Gray matter is comprised of neuronal cell bodies, unmyelinated axons and glial cells. The volume of gray matter is typically measured through voxel-based morphometry (VBM).

Hub: A hub is defined as a cluster of high degree nodes. Hubs play an important role in the network due to their high number of connections. Similar to a relay station within an electrical power grid, removing or damaging high degree nodes in the brain can wreak havoc on the system if they are eliminated.

Local efficiency (Eloc): Local efficiency measures the information transfer that may occur between nodes that are regionally close in proximity by computing the path length between a node and all of it’s nearest neighbors. High local efficiency implies that nodes tend to share information within their local region.

Module: Modules are community of nodes that have more interconnections to each other than to other nodes in other modules in the network. Another term used for module is community or neighborhood. For detailed information see Community Structure.

MEG: MEG is the abbreviated term for magnetoencephalography, a brain imaging technique that measures magnetic fields of brain activity by recording the magnetic field surrounding the electrical currents that naturally occur due to the signaling of neurons in the brain.

Network Science: A field of interdisciplinary science that has tools, techniques and a methodological approach for studying complex systems. A Network Science approach measures complex systems in terms of their components and the interactions between them. Network science techniques and methodology can be applied to a wide variety of systems in the physical and biological sciences. In brain imaging, components are nodes (voxels) and the edges are the connections between them. Network science is based on graph theory and, through the application of the techniques, can reveal how a system is structured and functions or behaves.

Node: A node is the basic component of the network. Nodes can be comprised of ‘things’ or people, or, in the case of brain imaging, a voxel of neurons.

Path length: The number of connections a node signal must pass through on the way to its destination node within the network. Often referred to by the symbol *L,* it is the number of steps that a node signal takes to transmit within the network.

Scale Free: In a scale-free network the degree distributions follow a power law where node preferentially attach to other high degree nodes. High degree nodes may be network hubs and will alter the network configuration such that the system may be driven or influenced by high degree nodes.

Simple Systems: A simple system is *homogeneous* and *weakly interactive*. Individual beliefs and expectations must be sufficiently uniform, and the level of interactions sufficiently weak or trivial, for us to be able to predict collective patterns of behavior with any confidence. Thus, a simple system is not emergent and the properties within the system can adequately predict the interaction outcome and behavior(s).

Small-World Network: A small world network is one that has nodes that neither display completely connected edges, nor randomly connected edges. A small world network is one that self-selects node connections; high degree nodes connect to other high degree nodes. The small-world phenomenon has been identified in many complex systems. For a more detail, see Watts and Strogatz (1998).

Task-Negative: A task-negative state is one where the mind is not actively involved in any sort of task. Tasks are considered anything from finger tapping to listening to music to paying attention to words or seeing pictures on a screen.

Voxel: A voxel is a pool of neurons in brain tissue. Voxels are acquired through fMRI data acquisition and are the basic components for fMRI data analyses. The number of neurons within an average voxel size of 3 x 3 x 3 mm^3 is estimated to be around 10^5 million.

White Matter Tracts: White matter tracts are fibers within the brain that are comprised of myelinated axons. White matter is measured through a technique called diffusion which can capture the direction of water molecules along the fiber tracts of the axons. White matter tracts are thought to contribute to overall healthy brain function by providing protective covering along the fiber tracts so that neuronal signal can propagate to other neurons. White matter degeneration is found to be significantly reduced in the brains of people diagnosed with diseases such as Parkinson’s and multiple sclerosis.