Musical Anhedonia and Individual Differences in Sensitivity to Music Reward

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Part I

The Evolution of Music
Chapter 1

It is difficult to nail down a time in history when music evolved; however, we do know it has been around for centuries. Almost two million years ago, the Homo ergaster was our first ancestor to walk upright, and this new anatomy moved the larynx lower down in the throat. At this point, early hominids were only capable of holistic, multi-modal, manipulative or musical vocalizations, known as the “Hmmm” communication system (Mithen, 2007). The evolution of bipedalism brought with it larger brains and an internal rhythm. A lower larynx allowed for the production of more diverse sounds. Although these evolutionary changes didn’t come about for musical purposes, they were the first steps in making music possible. Charles Darwin postulated that this newfound ability to sing and dance in early humans may have been used by males to seduce possible mates (Mithen, 2007). Fast forward to about 50,000 years ago when archaeologists uncovered the first musical instrument made from the femur bone of a bear (Huron, 2001). This ancient flute is the first evidence we have of the production of music; however, it’s likely that music evolved much earlier.

Why and how did music evolve? Why do we spend so much time, effort, and money to play it or listen to it? Does it hold evolutionary value, or is it just a frivolous stimulus useful only for recreation? Although music and language are largely connected, the evolution of language has been more thoroughly studied than the evolution of music. This may be due to the obvious evolutionary function of
language: the communication of information (Mithen, 2007). Language contributes greatly to our intellectual abilities and absolutely deserves the attention it has received, but the evolution of music and how it impacts our emotions has been wrongfully neglected in the research community.

Stephen Pinker, a psychologist and linguist, refers to music as “auditory cheesecake,” and postulates that it confers no evolutionary value (Pinker, 1997; Snowdon et al., 2015). As someone who spends a considerable amount of time studying music cognition, I am confident that this is an over-simplified argument. Charles Darwin argued that, since music holds no obvious survival benefit, it must be used in sexual selection (Charlton, 2014). Over 140 years later, Charlton produced data to support this claim, when he discovered that a woman’s menstrual cycle phase correlated with her sexual preference for composers that created more complex music (Charlton, 2014). Ian Cross also refutes Pinker’s argument, citing evidence that music is integral in the cognitive development of a child (Mithen, 2007). These explanations for the evolution of music rely on the hypothesis that music either does or does not hold evolutionary value, possibly making them too extreme. It is possible that the answer to this question lies somewhere in the middle. Altenmüller’s ‘Mixed Origins of Music’ hypothesis theorizes that music has many roots in early history, and evolved from an ancient affective signaling system. He argues that auditory learning in early humans, through chill responses to alarm calls or other auditory stimuli, was rewarded and led to the evolution of more refined auditory abilities (Altenmüller, 2013a). Aniruddh Patel, a neuroscientist and psychologist, argues that music is a
“transformative technology of the mind.” It elicits emotions and transforms our experience of the world (Patel, 2008a). I tend to agree with Patel; although music holds no obvious evolutionary benefit, I believe there is real merit in music’s ability to alter how we feel and how we interpret the world.

Music is universally valued because of its ability to elicit reward in several ways. It can be emotionally or socially rewarding, it can regulate our mood, and it can motivate us to move our body. I am interested in how the brain processes music, resulting in these rewarding experiences. In order to study this, I looked at a population that experiences no reward from music, musical anhedonics. Musical Anhedonia is defined as a specific lack of emotional response to music, despite intact emotional responses to other rewarding stimuli (Mas-Herrero et al., 2014). It is thought that a lack of auditory access to the reward system in the brain may cause this phenomenon. Functional MRI studies have shown that musical anhedonics have decreased functional connectivity between the right auditory cortex and the ventral striatum as compared to subjects with normal and enhanced sensitivity to music reward (Martinez-Molina et al., 2016). Listening to highly rewarding music, as indicated by how much a subject was willing to pay for it, is correlated with increased psychophysiological arousal, dopamine release in the striatum, and increased functional connectivity between the nucleus accumbens and the superior temporal gyrus (Salimpoor et al., 2009; Salimpoor et al., 2011; Salimpoor et al., 2013). It seems that the connection between these auditory and reward regions in the brain may explain the lack of music reward in these subjects with musical anhedonia. However,
it is possible that musical reward is a more complex process that involves other cortical and subcortical areas, like the limbic system and frontal cortices (Mas-Herrero et al., 2014). Previous case studies of acquired musical anhedonia reported lesions in temporal, frontal, and parietal regions, suggesting that the circuitry involved in music reward includes more than just auditory and reward regions (Mas-Herrero et al., 2014).

I plan to use different methodologies to study how the brain is processing music reward. I will use behavioral, psychophysiological, and both structural and functional MRI analyses to investigate this question, utilizing a case study of a severe musical anhedonic, as well as an analysis of individual variation in music reward sensitivity in the normal population. These differing methodologies should provide complementary data that can contribute to the bigger picture of music reward processing.
Part II

Experiments
Chapter 2

Behavioral Data

2.1 Subjects

BW is the name of our musical anhedonic; the control group consists of 46 Wesleyan students and community members. Each participant in this study was asked to complete a battery of behavioral surveys. These questionnaires were designed to not only examine music reward, but also to make sure that differences in reward sensitivity to music were not due to other confounding factors, like differences in intelligence, memory, general anhedonia, or musical ability. A questionnaire created by our lab found that BW did not differ significantly from controls in experience with musical training (average = 7.3 years (SD = 4.4yrs), BW = 4 years).

2.2 Baseline Tests

2.2.1 Shipley Institute of Living Scale

The Shipley Institute of Living Scale (Shipley, 1940) was given to test crystallized and fluid intelligence. The participants were asked to use prior knowledge and critical thinking to complete patterns in letters or numbers. This survey is used to show that the differences in music reward were not due to any differences in cognitive ability. The group average was 17.2/20 with a standard deviation of 1.91, showing that the participants in this study had normal intelligence. BW, our musical anhedonic, scored
15/20, meaning that his cognitive abilities are not significantly different from controls.

2.3 Tests of Musical Ability

2.3.1 Montreal Battery of Evaluation of Amusia

The MBEA 2 was given to our participants to check for tone deafness. The subjects were asked to listen to two consecutive musical excerpts, and report whether the excerpts were the same or different. We administered the second version of the MBEA, which “consists of a contour-violated alternate melody created by modifying the critical pitch so as to change the pitch direction of the surrounding intervals, while maintaining the original key” (Peretz et al., 2003). The average score on the MBEA, reported as a % correct, was 81.4% with a standard deviation of 6.83% in our control groups. BW scored an 80.6%, which translates to 25/31 correct. The average normal performance on the contour version of the MBEA in published norms, as shown in Table 2.3.1, is 27/30 or 90% correct, with a standard deviation of 2.2. This shows that BW’s score was relatively normal and differences in music reward in BW are not due to the inability to recognize musical tones.
Table 2.3.1: Mean correct responses on 30 trials of each test of the MBEA in 160 normal participants. Our subjects took the “Contour” version of this test (Peretz et al., 2003)

<table>
<thead>
<tr>
<th></th>
<th>Scale</th>
<th>Contour</th>
<th>Interval</th>
<th>Rhythm</th>
<th>Meter</th>
<th>Memory</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>27</td>
<td>27</td>
<td>26</td>
<td>27</td>
<td>26$^a$ (25)</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>SD</td>
<td>2.3</td>
<td>2.2</td>
<td>2.4</td>
<td>2.1</td>
<td>2.9$^a$ (3.5)</td>
<td>2.3</td>
<td>1.6</td>
</tr>
<tr>
<td>% of individuals with PF</td>
<td>17</td>
<td>9</td>
<td>7</td>
<td>15</td>
<td>14$^a$ (10)</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Cut-off score</td>
<td>22</td>
<td>22</td>
<td>21</td>
<td>23</td>
<td>20$^a$ (18)</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>% of N below cut-off</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1$^a$ (2)</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Note: N, normal participants; PF, perfect score; A, average. Cut-off scores correspond to 2 standard deviations below the mean.

$^a$Latest, harmonized, version of the test. Improvement over the prior nonharmonized version scores (shown in parentheses) is significant ($t_{158} = 2.332; P < 0.02$).

2.3.2 Pitch Discrimination Tasks

The pitch discrimination task (Loui et al., 2008) is a psychophysical perceptual task used to rule out tone-deafness. The test requires that a subject listen to two consecutive tones, and they must indicate if the second tone is higher or lower than the first. The task makes use of a three-up one-down staircase procedure (Cornsweet, 1962): As the participants report correct answers, the tones get closer together and the task gets more difficult. The task eventually converges upon the threshold, which is the lowest identifiable frequency difference around a 500 Hz center frequency.

Therefore, a lower score indicates a better performance. A score above 16 Hz indicates tone deafness. The average score on the pitch perception task was 6.69 Hz with a standard deviation of 7.59 Hz. BW scored 3.125 Hz on the pitch perception task. This score indicates that he is not tone deaf and has the ability to hear pitch differences at a lower frequency than most of the subjects.
2.4 Tests of General Reward

2.4.1 The Behavioral Inhibition System/Behavioral Approach System

The BIS/BAS survey (Carver, 1994) is used to test response to reward. The survey looks at a person’s behavioral approach system, which regulates a drive to obtain something desired. In opposition, the behavioral inhibition system (BIS) regulates a drive to avoid something unpleasant. The survey tests the sensitivity of these systems. The BAS is split into three subsections: drive (overall motivation to achieve), fun-seeking (willingness to do things for fun), and reward responsiveness (how one feels about reward). The BIS is not split into any subsections. BW showed higher scores than norms in the BAS drive, BAS reward, and BIS questions, indicating that he exhibits normal response to rewarding or aversive stimuli. The results of this survey are graphed in Figure 2.4.1.

![Figure 2.4.1: BW compared to normal scores on the BIS/BAS survey of reward in 4 categories](image_url)
2.4.2 The Physical Anhedonia Scale

The PAS (Chapman et al., 1976) looks for the existence of general anhedonia. Someone with general anhedonia would have trouble experiencing reward to most universally liked stimuli. This scale asks questions about reward to eating, movement, sex, smells, sounds, vision, and touch. The score of this test gets reported as a ‘% pathological,’ and we found that across our subjects, BW was the only participant showing pathological reward experience, and this pathology only existed for the questions pertaining to sound. This distribution is shown in Figure 2.4.2. Published norms for this scale can be found in Table 2.4.1, and they show that the controls in this study are very similar to the published norms and BW is significantly more pathological in the non-sound items as compared to our controls and the published norms.

![Figure 2.4.2: Scores on the Physical Anhedonia Scale, reported as either sound items or non-sound items](image-url)
Table 2.4.1: Published norms on the Revised Physical Anhedonia Scale for undergraduate students from three universities in North Carolina and the University of Wisconsin-Madison reported as % pathological (Chapman et al., 1976)

<table>
<thead>
<tr>
<th></th>
<th>NC African Americans</th>
<th>NC Caucasians</th>
<th>WI Caucasians</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Mean</td>
<td>17.85</td>
<td>16.11</td>
<td>13.6</td>
</tr>
<tr>
<td>SD</td>
<td>6.87</td>
<td>6.6</td>
<td>7.3</td>
</tr>
<tr>
<td>Alpha</td>
<td>0.77</td>
<td>0.8</td>
<td>0.83</td>
</tr>
<tr>
<td>Cut-off</td>
<td>31</td>
<td>29</td>
<td>28</td>
</tr>
</tbody>
</table>

2.5 Tests of Music Reward

2.5.1 The Barcelona Music Reward Questionnaire

The BMRQ (Mas-Herrero, 2013) measures sensitivity to music reward. The survey is split into five subcategories: music seeking, emotion evocation, mood regulation, sensorimotor, and social reward. The questions are phrased as statements and the participants must report the degree to which they agree with the statement. A question about social reward might be “When I share music with someone, I feel a special connection with that person” and an example of a sensorimotor question is “I don’t like to dance, not even with music I like.” BW scored more than five standard deviations below the mean music reward score of controls (average music reward score for controls = 49, SD=11.3, BW music reward score = -9). The data for the five subsection scores are graphed in Figure 2.5.1.
Figure 2.5.1: Results from the BMRQ shown in a radial graph. The controls group represents students from our study, while the norms group represents a group of 857 people who have previously taken this survey.

2.5.2 The Aesthetic Experience to Music Scale

The Aesthetic Experience Scale for Music (Sachs et al., 2016) asks questions about the different types of reward one might experience when listening to music. The questions range from more abstract reward (i.e. feeling like you’re somewhere else) to more visceral reward (i.e. getting chills). Multidimensional scaling on the responses to this questionnaire was performed in SPSS, and it produced Figure 2.5.2. The more abstract items end up in the right space and the more visceral items end up
in the left space on the plot. The distance between the dots indicates the likelihood that these two items are reported together.

Figure 2.5.2: Multidimensional Scaling solution of responses to the AES

2.5.3 Macquarie Battery of Emotional Prosody

The Macquarie Battery for Emotional Prosody (Thompson et al., 2012) tests for emotional perception of nonverbal sounds. This test was only administered to BW, as the other subjects reported no problem perceiving and feeling emotion in music. When listening to vocal, nonverbal bursts of emotion, BW correctly identified the
emotion of the sound 70% of the time. BW accurately predicted the emotion of a violin 90% of the time, and accurately predicted the emotion of a clarinet 87.5% of the time. This shows that BW can accurately perceive the appropriate emotion in different types of music and nonverbal sounds, even if he can’t feel them himself.
Chapter 3

Psychophysiological Data

3.1 Introduction

The behavioral surveys outlined in Chapter 2 inquire about several types of music reward, like music’s ability to regulate mood or the sensorimotor reward it evokes. In order to make a connection between brain and behavior, we rely on the assumption that the subjective ratings given on behavioral surveys do, in fact, correlate with objective brain differences. It has been suggested that a music-evoked change in emotional is what makes it pleasurable (Salimpoor et al., 2009). We conducted this smaller study with a separate cohort of subjects in order to provide a link between subjective ratings and physiological changes. We compare ratings of pleasure with changes in skin conductance when listening to emotionally charged music, with the hypothesis that a song reported as more pleasurable will induce greater skin conductance, or greater physiological arousal, in our participants. This would show that subjective ratings are representative of emotional arousal, so we could better trust that these ratings are reflective of objective differences in music reward experience.

3.1 Methods

3.2.1 Participants
Thirteen Wesleyan University students, 6 women and 7 men, were selected as subjects for this study (Table 3.3.1). Ten of these thirteen participants were obtained through a requirement of the Introductory Psychology class at Wesleyan University; the other three subjects volunteered. These participants were between the ages of 18 to 22, and gave written informed consent prior to the start of the study. BW, our musical anhedonic, also participated in this study.

3.2.2 Procedures

Each subject participated in a 2-hour session that included two major tasks. The first task is the music listening task, and the second task is participant screening, which consists of several surveys and tests.

3.2.3 Music Listening Task

A study by Sachs et al. (2016) identified thirteen songs that were reported as pleasurable and emotionally charged by multiple people, so we used these songs as our stimuli in the music listening task (Table 3.2.1). To measure galvanic skin response, each subject was fitted with NeuLog logger sensors secured with Velcro straps on the pointer and middle finger of the left hand (Figure 3.2.1). Baseline physiological data was collected over a 30-second period of silent relaxation before the task began. Then, while electrodermal activity was being recorded, each participant listened to an emotional portion of the song, which was usually around 90 seconds long. Testing was done in a sound attenuated room in the MIND Lab at
Wesleyan University. Music was played through both Sennheiser HD 280 Pro headphones and a pair of M-Audio BX5 D2 speakers. The NeuLog device records both GSR and sound, making it important to have the songs playing aloud from the speakers. The music listening task was recorded on a video camera. A program using Max/MSP played the songs in randomized order. The participants were asked to relax and focus on the way each song made them feel. While the subjects were listening, they were asked to record which ten-second window of the song represented the “peak emotional moment” using their right hand. They typed the time window in the text box shown on the program. After each song ended, the subjects were asked to rate the song on a scale from 0 to 4 (0 = dislike, 1 = neutral, 2 = low pleasure, 3 = high pleasure, 4 = chills) again using their right hand.

Table 3.2.1. List of songs used in the music listening task

<table>
<thead>
<tr>
<th>Song #</th>
<th>Artist</th>
<th>Song Name</th>
<th>Portion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Barber</td>
<td>Adagio for Strings</td>
<td>6:21 – 7:44</td>
</tr>
<tr>
<td>2</td>
<td>Adele</td>
<td>Someone Like You</td>
<td>2:19 – 3:52</td>
</tr>
<tr>
<td>3</td>
<td>Jeff Buckley</td>
<td>Hallelujah</td>
<td>4:37 - 6:12</td>
</tr>
<tr>
<td>4</td>
<td>Tchaikovsky</td>
<td>Symphony No. 6, mvmt 1</td>
<td>6:59 – 8:22</td>
</tr>
<tr>
<td>5</td>
<td>Death Cab for Cutie</td>
<td>I Will Follow You Into the Dark</td>
<td>1:27 - 3:02</td>
</tr>
<tr>
<td>6</td>
<td>Beethoven</td>
<td>Symphony No. 7, mvmt 2</td>
<td>5:25 – 6:52</td>
</tr>
<tr>
<td>7</td>
<td>Mahler</td>
<td>Symphony No. 2, Finale</td>
<td>13:24 - 14:48</td>
</tr>
<tr>
<td>8</td>
<td>Chopin</td>
<td>Nocturne in C Sharp Minor</td>
<td>2:29 – 3:56</td>
</tr>
<tr>
<td>9</td>
<td>Beethoven</td>
<td>Cavatina Op. 130</td>
<td>2:00 – 3:36</td>
</tr>
<tr>
<td>10</td>
<td>Rachmaninoff</td>
<td>Piano Concerto No. 2</td>
<td>0:01 – 1:28</td>
</tr>
<tr>
<td>11</td>
<td>Sufjan Stevens</td>
<td>John Wayne Gacy Jr</td>
<td>1:35 – 2:58</td>
</tr>
<tr>
<td>12</td>
<td>Johnny Cash</td>
<td>Hurt</td>
<td>0:14 - 1:39</td>
</tr>
<tr>
<td>13</td>
<td>Simon and Garfunkle</td>
<td>Sound of Silence</td>
<td>0:03 – 1:47</td>
</tr>
</tbody>
</table>
Figure 3.2.1: NeuLog apparatus used to measure of electrodermal activity. Real-time SCR was recorded from the pointer and middle fingers of the participants by NeuLog. It also simultaneously recorded the volume of music (in dB) played from the speakers.

3.2.4 Participant screening

After the music listening task, the participants completed a battery of tests. The Shipley test was administered to screen for cognitive impairment. Pitch perception and the Montreal Battery of Evaluation of Amusia (only 7 out of 13 participants took the MBEA) were given to assess the presence of tone deafness. The Digit Span Memory test was administered to measure short-term memory abilities. The Barcelona Music Reward Questionnaire (BMRQ) was given to assess emotional response to music and possibly the presence of musical anhedonia. The Physical
Anhedonia Scale evaluates general anhedonia. Lastly, the Aesthetic Experience Scale in Music (AES-M) was administered to measure emotional responses to music.

### 3.2.5 Data Analysis

In order to analyze the skin conductance changes during each song, we created a program on MATLAB2016 to analyze the skin conductance data. Over the course of the task, participants showed an upward trend in GSR, so our program de-trended the data. The program also produces an average GSR for each song, as well as a separate file for each song with the real-time skin conductance reported every 0.2 seconds. Microsoft Excel was used to analyze the average skin conductance of each participant during songs with different ratings.

SPSS was used to conduct a multivariate analysis and a principal components analysis from participants’ responses to AES-M. T-tests in SPSS were used to analyze the mean skin conductance for songs rated 4, or chills, compared to the other four options.

### 3.3 Results

#### 3.3.1 Psychometric scores

Twelve out of 13 participants were matched in age, IQ, ability to hear pitch differences, music reward sensitivity, and a lack of general anhedonia. One
participant (FWIC) met criteria for amusia (MBEA 20, Pitch Discrimination 34 Hz), and he also had a lower BMRQ score (Table 3.3.1). BW was not age matched to these participants, however he was matched in the results on the other behavioral surveys. A demographic table is shown in Table 3.3.1.

**Table 3.3.1. Participant demographics and Psychometric scores**

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>FWIC</th>
<th>BW</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>13</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td># of Females</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Age</td>
<td>19.1 (1.38)</td>
<td>19</td>
<td>53</td>
</tr>
<tr>
<td>Shipley Score</td>
<td>16.8 (2.22)</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Pitch Discrimination (Hz)</td>
<td>4.46 (2.92)</td>
<td>34</td>
<td>3.125</td>
</tr>
<tr>
<td>MBEA</td>
<td>26.3 (2.94)</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>BMRQ Scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musical Reward</td>
<td>54.0 (7.05)</td>
<td>37</td>
<td>-9</td>
</tr>
<tr>
<td>Music Seeking</td>
<td>55.8 (6.86)</td>
<td>49</td>
<td>13</td>
</tr>
<tr>
<td>Emotional Evocation</td>
<td>53 (9.40)</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>Mood Regulation</td>
<td>51.3 (10.5)</td>
<td>56</td>
<td>-1</td>
</tr>
<tr>
<td>Sensory-motor</td>
<td>47.6 (11.5)</td>
<td>43</td>
<td>12</td>
</tr>
<tr>
<td>Social Reward</td>
<td>58.5 (10.1)</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>PAS (% anhedonic score)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound Items</td>
<td>20.5% (15.5%)</td>
<td>45.50%</td>
<td>90.9%</td>
</tr>
<tr>
<td>Non-Sound Items</td>
<td>18.4% (6.64%)</td>
<td>51.50%</td>
<td>21.7%</td>
</tr>
</tbody>
</table>

**3.3.2 Music ratings and Electrodermal activity**

Data acquired from this study showed a positive association between subjective ratings of music and electrodermal activity. Figure 3.3.1 shows a graph of each participant’s average skin conductance when listening to songs with each of the five different ratings. Despite the intrinsic differences between participants’ GSR level, a
general trend is visible: an increase in GSR when listening to songs with higher ratings. However, the participant who met the criteria for amusia showed a decreasing pattern (FWIC). Furthermore, consistent with this participant’s low BMRQ and PAS scores, he did not rate any songs as chill inducing. In addition, BW’s skin conductance hovered around zero regardless of the rating he gave, which is consistent with his report that he experiences no emotional arousal from music.

Figure 3.3.1. Average Skin Conductance Rate by Song Rating. The X-axis indicates the ratings of participants. Each gray line is a participant, the blue dotted line represents the tone-deaf participant, and the red dashed line represents BW, our musical anhedonic. The black dashed line shows the average of the 12 normal participants.

A paired t-test revealed the differences between the mean GSR for those songs rated as chill inducing and those rated as dislike, neutral, low pleasure and high pleasure for
participants (Table 3.3.2). The GSR when participants reported chills was significantly different than when participants reported neutral, low pleasure, and high pleasure, while the GSR differences were not significant between chills and dislike. The lack of significant difference between songs rated as chills and dislike might be due to the fact that only two participants ever rated “dislike” for the music excerpts, thus preventing the statistical analysis of this pairing to be effective.

Table 3.3.2. Difference between GSR for chills and other ratings. Differences between GSR of songs rated as chills and neutral (p=0.011), chills and low pleasure (p=0.003), and chills and high pleasure (p=0.016) were significant.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Chills – Dislike</th>
<th>Chills – Neutral</th>
<th>Chills – LP</th>
<th>Chills – HP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>.82342</td>
<td>.47864</td>
<td>.54459</td>
<td>.37783</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>.79510</td>
<td>.34869</td>
<td>.43536</td>
<td>.40519</td>
</tr>
<tr>
<td>Std. Error Mean</td>
<td>.56222</td>
<td>.13179</td>
<td>.13767</td>
<td>.12813</td>
</tr>
<tr>
<td>95% Confidence Interval of the Difference</td>
<td>Lower</td>
<td>Upper</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-6.32030</td>
<td>7.96713</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>.15616</td>
<td>.80112</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>.23315</td>
<td>.85603</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>.08798</td>
<td>.66769</td>
<td></td>
<td></td>
</tr>
<tr>
<td>t</td>
<td>1.465</td>
<td>3.632</td>
<td>3.956</td>
<td>2.949</td>
</tr>
<tr>
<td>df</td>
<td>1</td>
<td>6</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Sig. (2-tailed)</td>
<td>.381</td>
<td>.011</td>
<td>.003</td>
<td>.016</td>
</tr>
</tbody>
</table>

3.4 Discussion

The results of this study show that there is a direct link between emotional arousal and ratings of pleasure. Each song had a range of different pleasure ratings, but the positive correlation between skin conductance and rating persisted regardless of the stimuli. These findings provide support for the theory that the pleasure we get from listening to music is directly related to physiological arousal (Salimpoor, 2009 #14). This is further proven by the skin conductance of BW, our musical anhedonic.
reports experiencing no emotional reward from music, and this is consistent with his skin conductance results. Regardless of his pleasure rating, BW’s skin conductance remained near zero, indicating that he was not emotionally aroused by any of the song stimuli. Taken together, these results prove that the subjective ratings given by our participants translate into objective music experience. Now that we know that these behavioral ratings correlate with physiological arousal, we can extrapolate that they are representative of actual music reward experience, providing validity for the results of our future MRI analyses.
Chapter 4

Diffusion Tensor Imaging Analysis
(This chapter was adapted from (Loui et al., 2017), a paper that I co-authored)

4.1 Introduction

Here we test the primary hypothesis that musical anhedonia reflects specific
differences in white matter connectivity within the reward system, and between the
auditory and reward systems. Secondly, we test the hypothesis that the same patterns
of white matter connectivity reflect individual differences in the normal variations of
reward experiences in music. Using combined behavioral and diffusion tensor
imaging (DTI) methods, we compare the white matter connectivity of a musically
anhedonic subject, BW, to a group of normal controls \( n = 46 \) who report a range of
reward from music. Results will identify the neuroanatomical networks that
predispose the human brain toward successful affective communication through
music.

4.2 Materials and Methods

4.2.1 Subjects

Subject BW (male, age 53 years, right-handed) presented with a self-reported,
socially debilitating lack of reward experience from music despite intact reward
responses to visual art. Table 4.2.1 shows demographic information and information about musical training. Screening measures including Montreal Battery for Evaluation of Amusia (Peretz et al., 2003) and the nonverbal measure of the Shipley Institute of Living Scale (Shipley, 1940) were used to rule out any differences due to amusia or general intellectual impairment, respectively.

Control subjects ($n = 46$, 17 females, all right-handed) consisted of Wesleyan students and community members. Subjects reported a variety of musical training, and tested within normal ranges for MBEA and Shipley (Table 4.2.1). Among the control subjects, 85% (39 subjects) completed the BMRQ. All subjects gave written informed consent as approved by the Institutional Review Boards of Wesleyan University and Hartford Hospital.
Table 4.2.1: Demographic information, baseline tests, and scores on BMRQ and PAS for BW and controls

<table>
<thead>
<tr>
<th></th>
<th>Control Group: Mean (SD)</th>
<th>BW</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>46</td>
<td>1</td>
</tr>
<tr>
<td># of Females</td>
<td>17</td>
<td>N/A</td>
</tr>
<tr>
<td>Age</td>
<td>20.5 (4.66)</td>
<td>52</td>
</tr>
<tr>
<td>Years of Musical Training</td>
<td>7.30 (4.44)</td>
<td>4</td>
</tr>
<tr>
<td>Age of Onset of Musical Training</td>
<td>8.35 (2.98)</td>
<td>13</td>
</tr>
<tr>
<td>Shipley Score</td>
<td>17.2 (1.91)</td>
<td>15</td>
</tr>
<tr>
<td>MBEA (% Correct)</td>
<td>81.4% (6.83%)</td>
<td>80.6%</td>
</tr>
<tr>
<td>BMRQ Scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musical Reward</td>
<td>49.0 (11.3)</td>
<td>-9</td>
</tr>
<tr>
<td>Music Seeking</td>
<td>53.4 (11.4)</td>
<td>13</td>
</tr>
<tr>
<td>Emotional Evocation</td>
<td>46.2 (13.3)</td>
<td>2</td>
</tr>
<tr>
<td>Mood Regulation</td>
<td>49.0 (12.2)</td>
<td>-1</td>
</tr>
<tr>
<td>Sensorimotor</td>
<td>44.3 (10.6)</td>
<td>12</td>
</tr>
<tr>
<td>Social Reward</td>
<td>55.4 (11.9)</td>
<td>24</td>
</tr>
<tr>
<td>PAS (% pathological score)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound Items</td>
<td>0.196%</td>
<td>0.909%</td>
</tr>
<tr>
<td>Non-Sound Items</td>
<td>0.196%</td>
<td>0.217%</td>
</tr>
</tbody>
</table>

4.2.2 Stimuli

In addition to screening tools reported above, 39 of the 46 subjects completed the Revised Physical Anhedonia Scale (PAS) (Chapman et al., 1976) and the Barcelona Music Reward Questionnaire (BMRQ) (Mas-Herrero, 2013). The PAS is a self-report scale used to measure anhedonia, the lowered ability to experience pleasure (Chapman et al., 1976). It consists of 61 statements that describe pleasurable experiences (e.g., “I have usually found lovemaking to be intensely pleasurable.”). Subjects are asked to indicate whether each statement is true or false as it applies to
them. Among the 61 statements, 10 items pertain to sounds (e.g., “The sounds of a parade have never excited me.”) whereas the others are non-sound items that include other sensory and social pleasures (e.g., “I have often found walks to be relaxing and enjoyable.” “I have often enjoyed receiving a strong, warm handshake.”).

The BMRQ (Mas-Herrero, 2013) was used to assess how BW experienced reward associated with music, in comparison with the control group. The BMRQ is a 20-item questionnaire designed to measure musical reward experiences as a combination of five factors: musical seeking, emotion evocation, mood regulation, sensory-motor, and social reward.

4.2.3 Procedures

After informed consent procedures, subjects completed surveys to report their demographic and musical training data. They also completed the MBEA and Shipley tests as screening measures for amusia and intellectual impairment. They then completed the PAS and BMRQ to assess possible general and musical anhedonia.

In addition to behavioral data, high-resolution T1 and DTI images were acquired in a 3T Siemens Skyra MRI scanner at the Olin Neuropsychiatry Research Center at the Institute of Living. Anatomical images were acquired using a T1-weighted, 3D, magnetization-prepared, rapid-acquisition, gradient echo (MPRAGE) volume acquisition with a voxel resolution of 0.8 mm × 0.8 mm × 0.8 mm. Diffusion images were acquired using a diffusion-weighted, spin-echo, echo-planar imaging sequence.
(TR = 4.77 s, voxel size = 2.0 mm × 2.0 mm × 2.0 mm, axial acquisition, 64 noncollinear directions with \( b \)-value of 1000 s/mm\(^2\), 64 noncollinear directions with \( b \)-value of 2000 s/mm\(^2\), 1 image with \( b \)-value of 0 s/mm\(^2\)).

4.2.4 Data Analysis

All MR images were processed using FMRIB’s Software Library (FSL) (Jenkinson et al., 2012). The images were then corrected for eddy current distortions using the eddy correct function. Non-brain structures were removed from each participant’s images by the brain extraction tool. A diffusion tensor model was fit at each voxel in the extracted brain using the dtifit function to get a fractional anisotropy (FA) image for each participant. Probabilistic tractography was conducted using a Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques (bedpostX) to determine the probable directions of each fiber for each brain voxel (Behrens et al., 2007).

Probabilistic tractography was conducted to determine structural connectivity in each hemisphere between each pair of the following regions of interest: STG, AIns, mPFC, and NAcc. The same regions were used as in our previous study (Sachs et al., 2016), as they were specifically identified to include white matter regions within the reward system (mPFC, NAcc, and AIns) and the auditory system (STG). The STG and NAcc were extracted from the Harvard-Oxford Cortical atlas (Desikan et al., 2006) and masked with a standardized FA image. The AIns was extracted from the LONI atlas.
(Shattuck et al., 2008). Then, using previous literature as a reference (Uddin and Menon, 2009), the anterior portion was defined anatomically within the lateral sulcus. As atlases varied in their delineation of the prefrontal cortex, the mPFC was hand drawn on coronal slices in the anterior portion of the corona radiata (Marchina et al., 2011). Each ROI was extracted or hand drawn on the standardized FA template by a first coder, and verified by a second coder. Each ROI was then warped to each individual subject’s FA image in native space and binarized.

Tractography was then initiated from each ROI as a seed toward each other ROI as a waypoint mask; and then tractography was initiated again using the original waypoint mask as the seed and the original seed as the waypoint mask; these two directions of probabilistic tractography were then averaged to yield a single tract between each pair of regions. Each resultant tract was averaged and then thresholded at 10% of its robust intensity level to minimize extraneous tracts. Tract volume and mean FA of the normalized tracts were exported for statistical comparisons. Additionally, to enable visualization all subjects’ tracts and FA images were aligned and normalized to the FSL 1 mm FA template using both linear registration (FLIRT) (Jenkinson and Smith, 2001) and nonlinear registration (FNIRT) tools, and canonical tract images were created by averaging each binarized tract across subjects in the control group, and thresholding voxels below the median.

One-sample $z$-tests were used to compare tract volume and normalized FA between BW and control group. Furthermore, to test for brain–behavior relationships within
the control group, we ran two separate multiple regression models, both using Music Reward (overall score from the BMRQ) as the dependent variable. The first regression used FA values from each tract as predictor variables; the second regression used volumes from each tract as predictor variables. Collinearity for all variables in both regressions was minimal (Tolerance > 0.1, VIF < 8). For tracts that were significant predictors of the Music Reward score, we also conducted follow-up tests for correlations between tract FA and each of the five subscores from BMRQ, while applying the Bonferroni statistical correction for the five subscores.

4.3 Results

4.3.1 Behavioral Results

Barcelona Music Reward Questionnaire showed that BW had low reward response to music in all categories of musical reward. While controls had an average factor score of 50 ($SD = 10$) on the BMRQ (Music Reward overall score), BW had an overall factor score of $-9$, which was 5.89 standard deviations below controls. BW scored more than 2.5 standard deviations below controls on all subscales of the BMRQ (Figure 2.5.1).

Physical Anhedonia Scale showed that BW was not generally anhedonic, except for items that pertain to sound. Control subjects generally scored an average of 17% of responses in the anhedonic (“pathological”) direction ($SD = 9\%$). BW scored a total of 39% of responses in the anhedonic direction. Item analysis of the PAS was done by
separately analyzing sound and non-sound categories. While the control subjects showed similar proportions of anhedonic scores for sound items and non-sound items ($M = 19.6\%, SD = 14\%$ anhedonic responses for sound items; $M = 16.8\%, SD = 11\%$ anhedonic responses for non-sound items); BW showed $21.7\%$ anhedonic scores for non-sound items (within $1$ SD of the mean) but $90.9\%$ anhedonic responses for sound items (more than $5$ SD above the mean). This striking dissociation (Figure 2.4.2) suggests that BW does not have general anhedonia, but is specifically anhedonic toward sounds, especially to music.

4.3.2 DTI Results

Musical Anhedonic vs. Controls

Figure 4.3.1 compares tract FA and volume between BW and control subjects, showing some differences in auditory–reward connectivity in the subject with musical anhedonia. BW had significantly lower tract volume than controls in tracts between the left STG and left NAcc ($z = −2.16, p = 0.03$) and between the left AIns and left NAcc ($z = −1.98, p = 0.04$) at the uncorrected $p < 0.05$ level. No other tracts showed statistically significant differences between BW and controls according to $z$-tests.

Mean FA (after normalizing for volume to enable a direct comparison of FA values) was greater for BW than controls between left STG and left NAcc ($z = 3.08, p = 0.002$), the same tract in which he showed lower volume than controls, surviving Bonferroni correction at $p < 0.05/10$. No other tracts showed significant differences in FA according to the $z$-test.
Figure 4.3.1: (a) Left: Mean FA of each tract comparing BW and controls, controlling for volume differences. **p < 0.05 Bonferroni-corrected (0.05/10 = 0.005). Right: Volume of each tract comparing BW and controls. *p < 0.05 uncorrected. (b) Averaged tract between STG and NAcc for controls (top row) and for BW (bottom row).
**Individual Differences within Control Group**

A multiple regression model with the dependent variable of Music Reward score, with tract volume (in mm\(^3\)) of each tract as predictor variables, accounted for 38% of the variability (\(R^2 = 0.38\)), but was not significant after accounting for the number of predictors (adjusted \(R^2 = 0.15\), \(F = 1.69\), \(p = 0.13\)). Among the controls, the Music Reward score was significantly predicted by the volume of tracts between LSTG and LAIns (\(\beta = 1.11, t = 2.76, p = 0.01\), bivariate correlation \(r = 0.26\), partial correlation \(r_p = 0.463\)), between RSTG and RNAcc (\(\beta = -0.81, t = -2.33, p = 0.027\), \(r = 0.036\), \(r_p = -0.40\)), and between RSTG and RMPFC (\(\beta = 0.74, t = 2.10, p = 0.045\), \(r = 0.193\), \(r_p = 0.37\)). Although these tract volumes were significant predictors of Music Reward at the \(p < 0.05\) level, they did not survive correction for multiple comparisons across the 10 tested tracts. *Figure 4.3.2* shows these tracts and scatterplots of their bivariate correlations with the Music Reward score.

A multiple regression model with the dependent variable of Music Reward score, with FA values of each tract as predictor variables, accounted for 26% of the variability (\(R^2 = 0.26\), adjusted \(R^2 = -0.002\), \(F = 0.99\), \(p = 0.47\)). None of the tracts emerged as significant predictors (all \(p > 0.05\)).

**Predicting Musical Anhedonic Brain and Behavior from Control Group Data**

To assess whether BW falls along the same continuum of brain–behavior relationships as predicted by controls, we first used the regression model from all tract volume data to generate a prediction for BW’s Music Reward score. Given the
multiple regression model obtained from tract volume data above (see section “Individual Differences Within Control Group”), BW’s tract volume data predicted his Music Reward score to be 0.29, which was much higher than his actual score (−9). However, pairwise correlations between behavior and tract volume (scatterplots in Figure 4.3.2) showed that BW is a predictable outlier from the control subjects’ data, with low volume in tracts between LSTG and LAIns and between RSTG and RMPFC, as predicted by his low Music Reward score and by control subjects’ data.

To assess whether BW’s tract volumes belonged to the same continuum as controls, we used the slope and intercept of the trend line that best fit the bivariate relationship among control subjects to predict BW’s tract volumes using his Music Reward score (Table 4.2.2), thus extrapolating control subjects’ data to predict BW’s tract volumes. The prediction fits BW’s actual data with 7.6% error for LSTG_LAIns tract, with 9.4% error for the RSTG_RNAcc tract, and with 1.0% error for the RSTG_RMPFC tract, suggesting that for these three tracts, BW falls on the extreme end of the same continuum as the control subjects.

Table 4.2.2: Predicting musical anhedonic from control data (Loui et al., 2017)
Figure 4.3.2: Volumes of tracts between left superior temporal gyrus (STG) and left anterior insula (top), between right STG and right nucleus accumbens (middle), and between right STG and right medial prefrontal cortex (bottom) were significant predictors of the Music Reward score among control subjects. Scatterplots show bivariate correlations ($r$) between Music Reward score and the volume of each tract, as well as partial correlation coefficients ($r_p$) from the regression for purposes of comparison against bivariate correlations. BW’s data are also shown on scatterplots for purposes of comparison.

4.4 Discussion

Individual differences in brain and behavior can be demonstrated by the normal variance within the general population, as well as extreme cases where substantial variations in brain and behavior give rise to striking deviations from the general
population. To the evolution of music, the existence of musical anhedonia presents one such model of a striking dissociation, in which some individuals have a lack of reward responses specifically to sound. Here, we see that patterns of white matter connectivity in the auditory and reward systems reflect individual differences in the tendency to perceive reward from music. Auditory–reward connectivity differences are observed in our extreme case of musical anhedonia, and also reflect individual differences in music reward sensitivity within the control group.

BW, a subject with severe musical anhedonia, had decreased white matter volume but higher FA between auditory and reward areas, specifically between left STG and left NAcc. The left STG is a cortical hub of the auditory system: it includes auditory belt and parabelt areas, which are important for analyzing temporal content of sounds, including speech-specific content (Overath et al., 2008; Overath et al., 2015). The NAcc is central to the mesolimbic pathway of the dopaminergic reward system, with its known role in reward and reinforcement (Wise, 2006), and is the crucial waystation of a reward network activated during the peak experience of music-related reward (Salimpoor et al., 2011; Zatorre and Salimpoor, 2013; Koelsch, 2014). Although the left NAcc showed higher volume of connectivity to the ipsilateral AIns as well as STG, the volume results were only significant at the uncorrected level; in contrast, the increased FA between left NAcc and STG was significant at the Bonferroni-corrected level in BW. FA, the main outcome variable in DTI, is an index of white matter integrity, which includes myelination and coherence of axonal bundles. Probabilistic tractography requires FA values of each voxel to be above the
white matter threshold, in order to derive tract volume (Behrens et al., 2007). Here, the pattern of simultaneously increased white matter integrity and decreased volume may suggest increased myelination and/or decreased crossing fibers in BW’s anatomical connections between LSTG and LNAcc, which could result in increased inhibition from LSTG to LNAcc. Functionally, the increased inhibition from LSTG could lead to a downregulation of the activity of LNAcc, resulting in deactivation of the NAcc as observed in recent functional MRI work in musical anhedonics (Martinez-Molina et al., 2016). Although these results are correlative rather than causal, the finding that BW had decreased volume but increased white matter integrity between these two regions adds to existing literature on the role of auditory–reward connectivity in affective responses for music (Salimpoor et al., 2013; Sachs et al., 2016); the implications of this data pattern for the evolution of music will be considered again later in this section “Discussion”.

The PAS showed that BW was anhedonic to all sound items, including non-music items (e.g., “the sounds of a parade”; “the cackling of fire in a fireplace”). Upon further interview, BW stated: “The crackle of a fireplace, the rustle of leaves, the swish of ocean waves – I just don’t appreciate them.” It remains to be seen whether musical anhedonics in other studies also report anhedonia toward sound items from the PAS, or whether BW is unique in his lack of appreciation of all auditory stimuli. If BW is different from other musical anhedonics in this regard, then one might expect that his auditory–reward disconnection is also more general than other cases of musical anhedonia.
Regarding the lack of appreciation for sounds, an interesting related question concerns whether BW could have misophonia, another auditory disorder where an individual reacts aversively to trigger sounds (Kumar et al., 2017). While more research is needed in the future to determine the extent of overlap or shared traits between misophonia and musical anhedonia, our study identifies BW as having musical anhedonia rather than misophonia, mainly because BW’s main complaint is that he feels no enjoyment from music, rather than being angered or anxious in response to trigger sounds as is common among misophonics (Edelstein et al., 2013). According to his self-report: “Music doesn’t particularly change my mood or give me an emotional response.” “Music never disgusts me. (The taste of cheese disgusts me. The smell of rotten eggs disgusts me. The sight of gore disgusts me.) Mostly I’d say that I’m neutral about music, because I just don’t care (and I don’t care that I don’t care!), and I mostly tune it out.” He also reports normal responses to speech and nonverbal vocal sounds. In contrast, misophonics most commonly report feeling disgusted, trapped, and/or anxious in response to trigger sounds, which are typically sounds produced by other people (Edelstein et al., 2013). From our findings, BW shows an abnormal pattern of connectivity from the NAcc; this was not observed in misophonics (Kumar et al., 2017). Thus, at present results suggest that musical anhedonia pertains more to a lack of reward, whereas misophonia pertains more to the experience of negative emotions such as anger and irritation in reaction to trigger sounds.

Within our control group, volume of some tracts between auditory and reward
regions, specifically between LSTG and LAIns, between RSTG and RNAcc, and between RSTG and RMPFC, were predictive of musical reward at the 0.05 (uncorrected) level. Although these results do not survive correction for multiple comparisons, it is noteworthy that only tracts from left or right STG (the only auditory regions in our model) emerged as significant predictors, suggesting that individual differences in music reward do pertain to auditory-specific access to the reward system. It is also noteworthy that BW’s tract volume data can be predicted by extrapolating the trend line that best fits the bivariate relationship between music reward and volume of the significant predictor tracts. In contrast, the multiple regression model obtained from control subjects did not accurately predict BW’s music reward score. Thus, control subjects’ data can predict BW’s tract volumes but not his behavioral scores. This may be because BW’s music reward score, at 5.89 SD below controls, is much more of an outlier than his brain measures; thus, the brain predictors of behavior derived from control subjects do not apply to BW’s very unusual behavioral data, but BW’s tract volume data appear to lie at the low end of a normal distribution. The fact that BW is a very extreme outlier on the BMRQ also suggests that true musical anhedonia, at least as represented by the case of BW, is probably very rare. This is consistent with the observation that across patients of many types of brain damage, few report musical anhedonia (Belfi et al., 2017). Future studies might rely on more targeted strategies to identify more such cases of musical anhedonia.

The tract between LSTG_LAIns shows a continuum in volume that best reflects our
range of behavioral data: its volume is reduced in the musical anhedonic as well as positively correlated with music reward. Connections between AIns and STG likely include the arcuate fasciculus, part of the auditory dorsal pathway that connects superior temporal and inferior frontal regions that is related to musical ability (Loui et al., 2009; Halwani et al., 2011; Loui et al., 2011; Loui, 2015). Furthermore, AIns is reduced in functional connectivity to auditory cortex in singers (Kleber et al., 2013), and functional connectivity between LSTG and LAIns is correlated with lexical retrieval in spontaneous speech (Chai et al., 2016). In addition to its role in vocal–motor integration and speech, the AIns is part of the classic limbic system and is implicated in the quartet theory of emotions due to its importance in interoception and emotional regulation (Koelsch, 2014). Given these diverse roles of AIns in the auditory–motor system, the present finding of increased tract volume between left AIns and LSTG in controls who experience high musical reward may relate to auditory–motor behavior especially as it applies to vocal–motor behavior. This auditory–insula connectivity may be related to the differentiation of vocalization repertoire as posited in the MOM theory (Altenmüller, 2013a). The MOM theory states that differentiation of vocalization repertoire, as driven by chill experiences, led to the capacity for fine-grained rhythmic–melodic discrimination. In our evolutionary history, it is possible that individuals with high LSTG_LAIns connectivity, who were highly reward-sensitive to music (e.g., frequently experiencing chills in response to music), then went on to acquire fine-grained auditory discrimination skills, which then gave rise to language and music. Since the AIns is an evolutionarily older part of
the brain than its neighbor the inferior frontal gyrus (which is a classic endpoint of the arcuate fasciculus) (Galaburda, 1982; Semendeferi and Damasio, 2000), the LSTG_LAIns connection could have predated the arcuate fasciculus, thus serving as a pathway for the differentiation of vocalization response that preceded the hypothesized bifurcation of auditory information into music and language (Mithen, 2007).

Superior temporal gyrus connections to NAcc and mPFC may include the arcuate as well as the uncinate fasciculus, the latter being part of the auditory ventral pathway that connects the temporal and frontal lobes (Wakana et al., 2004) and is involved in processing local syntactic structures (Friederici, 2009). mPFC is also part of the default mode network and is involved in social, self-referential, and emotional processing (Fox et al., 2005; Mason et al., 2007; Jenkins and Mitchell, 2010; Kim and Johnson, 2015). As the mPFC is a waystation of the dopaminergic system that probably emerged later in evolution (Galaburda, 1982; Semendeferi and Damasio, 2000), the finding that connections to it correlate with musical reward suggests a further involvement of an evolutionarily younger part of the dopaminergic system in music processing beyond the NAcc. Interestingly, while the LSTG_LAIns and LSTG_LMPFC tracts show positive bivariate as well as significantly positive partial correlations to music reward, the RSTG_RNAcc tracts show no significant bivariate correlation with music reward, but a significant negative partial correlation after partialling out the effects of the other predictors. This is especially intriguing when considered alongside data from the musical anhedonic subject: BW had a lower
volume but higher FA in LSTG_LNAcc; highly hedonic controls had lower volume
in RSTG_RNAcc. Together these results suggest that auditory access to the
mesolimbic pathway is hemispherically asymmetric, with normal variations in reward
sensitivity occurring on the right but abnormal lack of reward on the left. This is
consistent with hemispheric asymmetry to attractive vs. aversive stimuli in animals,
but only in learned responses (Besson and Louilot, 1995; Molochnikov and Cohen,
2014). In light of the MOM theory, which posits that chill responses were initially a
reward to novel auditory patterns prior to its driving of differentiated vocalization
repertoire as discussed above, the present findings link the STG_NAcc pathway to
this very early step in the evolution of music.

While this study cannot tease apart when or how these individual differences
emerged, the pattern of results can be considered in the context of known steps in
brain evolution as well as development, which together provide support for the MOM
theory. Our rare case of musical anhedonia possesses a different pattern of white
matter pathways between auditory regions and reward-sensitive regions, possibly due
to abnormal neuronal migration in utero or early in development. In the multiple
regression analysis to predict musical reward scores from diffusion measures, since
we tested pairwise connections between regions in the auditory and reward networks,
this necessarily resulted in an elevated number of statistical comparisons. The brain–
behavior relationships within the control group are only significant at the uncorrected
level. Thus, although the current results are interesting they should be interpreted
cautiously until further verification. Nevertheless, the FA difference between BW and
the control in the LSTG–NAcc tract survives correction for comparisons across the 10 tested tracts; this gives us higher confidence in a structural difference between auditory and reward areas that is linked to musical anhedonia.

A remaining question concerns whether musical anhedonia is likely to be a spectrum disorder. The answer to this question depends on how we define musical anhedonia. Considering that the BMRQ is for now the only diagnostic tool explicitly in use to identify musical anhedonia, and it yields a continuum of scores when administered to a large population (Mas-Herrero et al., 2014), the lack of musical reward appears to be continuously distributed. On the other hand, if we define musical anhedonia by self-identification of a socially debilitating lack of reward experiences specific to music, then it might not be a spectrum. However, defining musical anhedonia by self-identification would mean that identification depends upon the subject’s awareness of their own condition, which would in turn depend on their social environment. For instance, if BW had not heard about musical anhedonia, or if he lived in an environment where music was less celebrated, then he might not have become aware of his condition. Thus, large-scale testing of musical reward sensitivity across different cultures may be helpful for future definitions of cultural norms against which we define musical anhedonia.

Results show that musical anhedonia is related to different patterns of connectivity from auditory to emotion and reward centers of the brain. This auditory access to the reward system informs the evolutionary basis of music: perhaps music evolved as a
direct auditory pathway toward social and emotional reward centers in the brain.

With regard to the shared evolutionary basis of music with language, it is worth noting that in contrast to music, language does not seem to achieve the same set of evolutionary functions; that is, although language and music both involve connectivity between auditory, motor, and cognitive systems, language has more direct and specific sound-to-meaning mappings, but music more readily establishes aesthetic or emotional connections such as chills (Silvia et al., 2011). Thus, language and music may have shared evolutionary origins as a protolanguage (Mithen, 2007), but their divergence led to different evolutionary functions and outcomes.

Successful musical communication depends on an auditory channel through which reward and emotional areas can be accessed. This is consistent with views of music as mixed origins, which posits that music evolved from evolutionarily ancient chill reactions to affiliative sounds (Altenmüller, 2013b) that then transform the mind (Patel, 2008a). Evolutionarily, the emotional content of sound might have accessed these auditory–reward pathways, which then predisposed the brain toward developing reward sensitivity and thus the need for successful emotional communication. In that regard, results suggest that other species who have connectivity between auditory and reward systems would also be able to enjoy music given the appropriate exposure.

Previous work on congenital amusia has been discussed in terms of its implications on the evolution of music (Patel, 2008a); in particular white matter connectivity in congenital amusia supports the hypothesis for a shared basis of music and language
(Loui et al., 2009; Loui, 2015). Similarly, white matter connectivity in musical anhedonia informs the evolutionary basis of music on emotion. While reward pathways and auditory perception–action pathways are conventionally seen as separate and dissociable systems in the brain, the present study suggests that they operate in concert, and that this concert of brain systems may be important for the evolution of music: in fact, they may provide support for the MOM as tools to transform the mind (Kleinman, 2015).

Individual differences in structural connectivity between the auditory and reward networks likely represent normal variation in musical reward sensitivity, with some additional patterns that give rise to extreme cases such as musical anhedonia. While increased connectivity between auditory and reward networks is indicative of intense emotional responses to music such as frissons (Harrison and Loui, 2014; Sachs et al., 2016), decreased volume coupled with increased myelination or coherence between specific nodes of these networks reflects the striking lack of specific emotional responses as observed in musical anhedonia. By distinguishing between common variations and rare extremes in individual differences in musical reward sensitivity, the present study attempts to extend the MOM theory by identifying distinct neural pathways through which music might operate as an affective signaling system.
Chapter 5

Resting State fMRI

5.1 Methods

5.1.1. Subjects

All but seven of the subjects in the DTI analysis were utilized for the rsfMRI analysis. A demographic table can be viewed in Table 5.1.1. These data look very similar to the data found in Table 4.2.1, as the majority of the subjects were used in both analyses.

Table 4.2.1: Demographic table

<table>
<thead>
<tr>
<th></th>
<th>Control Group; Mean (SD)</th>
<th>BW</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>39</td>
<td>1</td>
</tr>
<tr>
<td># of Females</td>
<td>16</td>
<td>N/A</td>
</tr>
<tr>
<td>Age</td>
<td>21.0 (4.60)</td>
<td>52</td>
</tr>
<tr>
<td>Years of Musical Training</td>
<td>7.56 (4.60)</td>
<td>4</td>
</tr>
<tr>
<td>Age of Onset of Musical Training</td>
<td>7.94 (2.85)</td>
<td>13</td>
</tr>
<tr>
<td>Shipley Score</td>
<td>17.2 (1.91)</td>
<td>15</td>
</tr>
<tr>
<td>MBEA (% Correct) (n=26)</td>
<td>81.4% (6.83%)</td>
<td>80.6%</td>
</tr>
<tr>
<td>BMRQ Scores (n=33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musical Reward</td>
<td>48.4 (11.2)</td>
<td>-9</td>
</tr>
<tr>
<td>Music Seeking</td>
<td>52.0 (11.7)</td>
<td>13</td>
</tr>
<tr>
<td>Emotional Evocation</td>
<td>46.5 (12.4)</td>
<td>2</td>
</tr>
<tr>
<td>Mood Regulation</td>
<td>48.9 (12.2)</td>
<td>-1</td>
</tr>
<tr>
<td>Sensorimotor</td>
<td>43.7 (10.3)</td>
<td>12</td>
</tr>
<tr>
<td>Social Reward</td>
<td>54.5 (11.9)</td>
<td>24</td>
</tr>
<tr>
<td>PAS (% pathological score)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound Items</td>
<td>0.196%</td>
<td>0.909%</td>
</tr>
<tr>
<td>Non-Sound Items</td>
<td>0.196%</td>
<td>0.217%</td>
</tr>
</tbody>
</table>
5.1.2. Data acquisition and analysis

The resting state fMRI images were obtained in a 3T Siemens Skyra MRI scanner at the Olin Neuropsychiatry Research Center at the Institute of Living. The scans were acquired sagittally in 947 volumes over 7 minutes (TR = 475 ms), and the voxel resolution was $3 \times 3 \times 3 \text{mm}^3$. Data processing was conducted by FEAT (FMRI Expert Analysis Tool) Version 6.00, which is part of FSL (FMRIB’s Software Library, www.fmrib.ox.ac.uk/fsl). Brain Extraction Tool, or BET, was used to remove any non-brain signal. FLIRT (FMRIB’s Linear Image Registration Tool) was used to translate these rsfMRI images to high-resolution structural images or standard images (Jenkinson and Smith, 2001; Jenkinson et al., 2002). FNIRT (FMRIB’s Nonlinear Image Registration Tool) was used to further refine this process (Andersson, 2007a, 2007b). The FEAT program applied pre-statistics to these images including: MCFLIRT (Jenkinson et al., 2002), BET (Smith, 2002), spatial smoothing using a Gaussian kernel of FWHM 8.0mm, grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0s), and removal of white matter and CSF confounds.

ROI selection was informed by the previous DTI study. The nucleus accumbens (NAcc) was still used as a reward region, and the Anterior Insula (AIns) was maintained as a region involved with emotion and reward. However, we decided to include a few extra ROIs in this analysis. We split the Superior Temporal Gyrus (STG) into an anterior, middle, and posterior region, as we hypothesized that these
regions may contribute differently to music reward. We also considered the entire STG (combination of all three regions) as its own ROI. This analysis also included the Superior Temporal Sulcus (STS) as an ROI because it has been cited as a region that is specific to the pathway for music processing (Norman-Haignere et al., 2015). The orbitofrontal cortex was also included as a reward region, and both divisions of the inferior frontal gyrus (pars triangularus and pars opercularis) were used as auditory-motor regions. These regions of interest were drawn using the Harvard-Oxford Atlas (Desikan et al., 2006) and are depicted in Figure 5.1.1.

Figure 5.1.1 – ROIs selected for the rsfMRI analysis. ROIs above the blue line are emotion/reward regions, and ROIs below the blue line are auditory/motor regions.

Timecourses were extracted for all 20 ROIs, and timeseries correlations of the ROIs were performed across all 40 subjects using MATLAB. A z-test in MATLAB was used to compare the average timeseries correlations across the 39 control subjects to the timeseries correlations in BW for each ROI. The overall music reward score
from the BMRQ and the factor scores from the Aesthetic Experience Scale for Music (produced from a principle component analysis on SPSS) were correlated with the timeseries correlations using MATLAB.

### 5.2 Results

BW’s timeseries correlations for each ROI are represented by the plot in Figure 5.2.1a. The timeseries correlations of the 39 control subjects for each ROI are represented by the plot in Figure 5.2.1b. The results of the z-test comparing these two plots is shown in Figure 5.2.1c. Only three correlations were significantly decreased in BW as compared to the control group (a z-score less than -2). The correlation between the LOFC and the LIFG pars triangularis (Z-score = -2.0293), the RSTS with the entire RSTG (Z-score = -2.4674), and the RSTS with the anterior RSTG (Z-score = -2.6170). However, I suspect that the significant correlation between the RSTS and entire RSTG is driven by the correlation specifically between the anterior portion of the RSTG with the RSTS.
The fact that these regions were significantly less correlated in BW than in controls is interesting, and may contribute to his difficulty experiencing reward from music. To look into this further, I examined individual variation in music reward in the control population. First, I correlated the overall music reward score from the BMRQ with the timeseries correlations of the 34 participants who had taken the BMRQ to see how this variation is associated with resting brain connectivity. I found that the correlation between the RSTS and the RNAcc was significantly associated.
with Music Reward Score (Figure 5.2.2). Subjects that are more sensitive to music reward have a greater correlation between these auditory and reward regions.

![Scatter plot showing the significant association between music reward score on the BMRQ and the correlation between the RSTS and the RNAcc](image)

Figure 5.2.2 – Scatter plot showing the significant association between music reward score on the BMRQ and the correlation between the RSTS and the RNAcc

Next, we performed a principal components analysis on the scores from the Aesthetic Experience Scale for Music. This analysis produced two components: the first of which loads highly on all of the questions from this scale and the second loads highly on questions that reference more visceral reward from music. In other words, a high Factor 1 score would indicate that a subject experiences greater emotional responses to music in general, while a high Factor 2 score would indicate that the subject gets more visceral, rather than abstract, reward from music (Table 5.2.1). None of the correlations were significantly associated with the Factor 1 score from the AES-M, but several correlations were significantly correlated with Factor 2 scores.
(Table 5.2.2). The two most significant associations were found in the correlations between the RAIns and the RIFG pars opercularis ($r(32) = -0.5004, p = 0.0035$) and also between the RAIns and the middle division of the RSTG ($r(32) = -0.4834, p = 0.0051$). Because these are negative correlations, this suggests that a lower Factor 2 score (more abstract music reward) is associated with a greater correlation between these reward & auditory/motor ROIs (Figure 5.2.3).

Table 5.2.1 – The two components, or factors, that came out of the principal components analysis.

<table>
<thead>
<tr>
<th>Item</th>
<th>Factor 1</th>
<th>Factor 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>absorbed</td>
<td>0.703</td>
<td>-0.489</td>
</tr>
<tr>
<td>lose-time</td>
<td>0.688</td>
<td>-0.328</td>
</tr>
<tr>
<td>chills</td>
<td>0.816</td>
<td>0.084</td>
</tr>
<tr>
<td>goosebumps</td>
<td>0.774</td>
<td>0.17</td>
</tr>
<tr>
<td>somewhere-else</td>
<td>0.744</td>
<td>-0.065</td>
</tr>
<tr>
<td>hair-on-end</td>
<td>0.752</td>
<td>0.285</td>
</tr>
<tr>
<td>crying</td>
<td>0.674</td>
<td>0.21</td>
</tr>
<tr>
<td>touched</td>
<td>0.739</td>
<td>-0.326</td>
</tr>
<tr>
<td>detached</td>
<td>0.63</td>
<td>-0.166</td>
</tr>
<tr>
<td>awe</td>
<td>0.705</td>
<td>-0.309</td>
</tr>
<tr>
<td>lump-in-throat</td>
<td>0.658</td>
<td>0.479</td>
</tr>
<tr>
<td>pit-of-stomach</td>
<td>0.705</td>
<td>0.424</td>
</tr>
<tr>
<td>heart-racing</td>
<td>0.638</td>
<td>0.158</td>
</tr>
<tr>
<td>heart-skip-beat</td>
<td>0.665</td>
<td>0.374</td>
</tr>
<tr>
<td>strong-emo-resp</td>
<td>0.754</td>
<td>-0.447</td>
</tr>
</tbody>
</table>
**Table 5.2.2:** All of the timeseries correlations that were significantly associated with Factor 2 scores with their corresponding r and p values.

<table>
<thead>
<tr>
<th>Correlation</th>
<th>r-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAIns_RSTG (div 2)</td>
<td>-0.3732</td>
<td>0.0354</td>
</tr>
<tr>
<td>LAINS_LIFG (posterior)</td>
<td>-0.377</td>
<td>0.0334</td>
</tr>
<tr>
<td>RAINS_LSTG (div 2)</td>
<td>-0.3693</td>
<td>0.0375</td>
</tr>
<tr>
<td>RAINS_LSTG (div 3)</td>
<td>-0.3624</td>
<td>0.0415</td>
</tr>
<tr>
<td>RAINS_LSTG (all)</td>
<td>-0.3694</td>
<td>0.0375</td>
</tr>
<tr>
<td>RAINS_RSTG (div 2)</td>
<td>-0.4834</td>
<td>0.0051*</td>
</tr>
<tr>
<td>RAINS_RSTG (all)</td>
<td>-0.4043</td>
<td>0.0217</td>
</tr>
<tr>
<td>RAINS_RIFG (anterior)</td>
<td>-0.4014</td>
<td>0.0228</td>
</tr>
<tr>
<td>RAINS_RIFG (posterior)</td>
<td>-0.5004</td>
<td>0.0035**</td>
</tr>
<tr>
<td>LOFC_LIFG (anterior)</td>
<td>-0.3568</td>
<td>0.045</td>
</tr>
<tr>
<td>LOFC_LIFG (posterior)</td>
<td>-0.4074</td>
<td>0.0206</td>
</tr>
<tr>
<td>RSTG (div 1)_RIFG (posterior)</td>
<td>-0.3669</td>
<td>0.388</td>
</tr>
<tr>
<td>RSTG (div 2)_RIFG (posterior)</td>
<td>-0.4038</td>
<td>0.0219</td>
</tr>
<tr>
<td>RNAC_LSTG (div 1)</td>
<td>-0.3494</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**Diagram:**

```
plot()

# Example code for reproducible plot
plot(aes(x = AES Factor 2 Score, y = pRIFG_RAIns), data = your_data)
geom_point() + geom_smooth(method = "lm")
```
5.3 Discussion

At rest, BW’s brain is significantly less correlated between the LOFC and anterior LIFG, the RSTS and anterior RSTG, and the RSTS and entire RSTG. These differences were unexpected as they did not include any decreased correlations between auditory and reward regions. Using BW as a case study that we compare to controls is a useful way to investigate the neural correlates of Musical Anhedonia; however, BW may just lie on the extreme end of a spectrum of sensitivity to music reward. To get a better look at how the brain processes music reward, we can look at...
the variation in scores on the BMRQ and AES-M in the normal population and correlate those scores with resting brain connectivity patterns. Music reward scores on the BMRQ were significantly associated with the correlation between the RSTS and RNAcc. The RSTS is a major auditory region and the RNAcc is a hub of the reward network, so it makes sense that subjects with lower BMRQ scores would have a decreased correlation between these two regions, while the opposite would be true of subjects with enhanced music reward. Factor 2 scores on the AES-M were significantly associated with several timeseries correlations, including the ones between the RAIns and posterior RIFG and the RAIns and middle RSTG. These correlations were negative, meaning that a subject with a lower Factor 2 score would have an increased correlation between these regions. A lower Factor 2 score indicates that the subject experiences more abstract reward from music, so it’s possible that the correlations between these regions are involved in more conceptual processing of music reward.
Part III

Conclusions
Using different methodologies to study the how the brain processes music reward should provide complementary information to answer that question. A comparison of these different methods may add to our understanding of how structural and functional connectivity are contributing to these individual differences in music reward. First, it’s important to understand how these differing technologies work and what they can tell us about brain connectivity.

Diffusion Tensor Imaging relies on the idea that water diffuses down the major direction of an axon (Basser and Jones, 2002). This directed diffusion of water in white matter is in contrast to the diffusion of water in other, less constrained brain regions. For example, water molecules in cerebral spinal fluid can diffuse in any direction, and can be characterized as isotropic (Basser and Jones, 2002). We can visualize the direction of these water molecules by applying diffusion gradients in at least six non-collinear, non-coplanar directions; this gives us enough information to calculate a diffusion tensor for each voxel in the brain space (Basser and Jones, 2002). These tensors have three eigenvectors associated with them that form a diffusion ellipsoid. The main eigenvector is the largest one and indicates the direction of the tract in question, and the other eigenvalues represent the other axes in the ellipsoid (Basser and Jones, 2002). The degree to which diffusion is constrained to a single direction is measured by the fractional anisotropy or FA (Basser and Jones, 2002). An FA value of 0 means the tensor is completely isotropic and an FA value of 1 means the tensor is constrained to only one direction. A tensor with a higher FA would have a larger main eigenvector and the second and third eigenvalues would be
relatively small in comparison, making the ellipsoid more elongated in the direction of the tract. FA is a measure of white matter integrity, which represents the strength of the connection in the tract, but this could arise in many different ways. Increased FA could be due to extra myelination, more coherent axon fibers, or decreased crossing fibers (Basser and Jones, 2002). We used both tract volume and FA to measure the strength of the connections between our ROIs. These white matter differences have been shown to correlate directly to variation in behavior (Johansen-Berg, 2010), suggesting that the observed volume and FA differences could be used to explain the behavioral differences in BW when compared to controls.

Resting state fMRI relies on a different brain mechanism; it uses spontaneous blood oxygen-level dependent (BOLD) signals at rest to measure task-independent changes in brain function (Guerra-Carrillo et al., 2014). BOLD signals are visualized by measuring the ratio of oxygenated to deoxygenated hemoglobin at an ROI, with the assumption that a more activated region will experience increased blood flow and glucose consumption, which, in turn, will increase that ratio (Fox and Raichle, 2007). Previous research on functional connectivity in the brain has focused on task-dependent signaling, attempting to average out the spontaneous “noise”; however, only 5% of the energy our brain uses can be attributed to task-related changes in brain metabolism, meaning that research has neglected the mechanism that is using the majority of the brain’s energy: spontaneous activity (Fox and Raichle, 2007). Long-term potentiation is the idea that the brain has the ability to form new experience-dependent connections. In turn, correlations between ROIs at rest suggest a prior
history of co-activation (Guerra-Carrillo et al., 2014), allowing us to assume that
regions that are highly correlated experience similar activation patterns at rest. In our
experiment, we chose 20 relevant ROIs and looked at the correlations of each ROI
with the other nineteen. We can use these data to compare the strength of timeseries
correlations to scores on music reward questionnaires to make a conclusion about
how resting brain connectivity results in a specific music reward experience.

When using BW as a case study and comparing his brain to controls, the DTI
analysis found that the tract between the LNAcc and LSTG had significantly greater
FA and significantly lower volume in BW than in controls. These results are
contradictory, and may signify that BW has increased myelination or decreased
number of crossing fibers in that tract. In general, the tract between these left auditory
and reward regions is different in BW than in controls and may contribute to his
difficulty experiencing reward from music. The rsfMRI analysis found that the
correlation between the LOFC and LIFG pars triangularis, the RSTS and entire
RSTG, and the RSTS and anterior RSTG were significantly decreased in BW as
compared to controls. These results were interesting and differed from the results of
the DTI analysis; the decreased frontal-to-frontal and auditory-to-auditory
correlations were not expected and suggest that structural and functional connectivity
contribute differently to music reward processing.

These differences between BW and controls are not due to differences in
musical training, as BW did not differ significantly from the group in number of years
of musical training. These differences are also not due to the presence of amusia or
general anhedonia. BW experiences normal reward from stimuli other than music, suggesting that this anhedonia is specific to music. One major difference between BW and controls is his age. BW is 53 years old, while the average age of control subjects was 20.5 years old. Brain volume decreases with age, but we controlled for brain volume in the DTI study, so the tract volume differences cannot be attributed to an overall decrease in brain volume in BW. We also normalized the functional ROIs to the subjects’ brains in the rsfMRI study; thus the functional connectivity differences we found also cannot be attributed to overall differences in brain volume. Therefore, we can assume that these differences in structural and functional connectivity in BW can explain his decreased sensitivity to music reward.

We also used these different methodologies to study individual variation in the normal population. In the DTI study, the volume of the tracts between the LSTG & LAIns, the RSTG & RNAcc, and the RSTG & RMPFC was significantly correlated with music reward scores on the BMRQ. The rsfMRI analysis found that the timeseries correlation between the RSTS and the RNAcc was significantly associated with music reward score. Although these implicated regions aren’t exactly the same across techniques, it’s promising that both the structural and functional connectivity between auditory and reward regions are correlated with music reward score.

The results from both the DTI and rsfMRI analysis suggest that connectivity between auditory and reward regions are underlying the differences observed in sensitivity to music reward, and may explain the severe case of musical anhedonia.
seen in BW. The reward regions included in these analyses utilize the dopaminergic system in our brain to process rewarding stimuli, and these results suggest that music can activate this dopaminergic system and result in reportedly rewarding experiences. This reward system evolved before our specific cortical systems for both music and language (Patel, 2008b). There is overwhelming evidence that humans evolved through natural selection to have the ability of language, but this is not the case for music. However, music and language have a lot of overlapping cortical structures in the brain, and they utilize many of the same functional resources (Patel, 2008b).

Language evolved for the purpose of better communication, but it is less clear why music came to be. Although no definitive answer exists to this question, music is a human invention that has the ability to transform someone’s experience (Patel, 2008a, 2008b). We don’t have enough evidence to conclude that music evolved as a biological adaptation, but we also can’t diminish it to “auditory cheesecake” (Pinker, 1997) as it has the ability to change a person’s life. It is this quality of music that makes it critical to understand, and musical anhedonia is an ideal model system to study the reward pathways that give music its power.
Part IV

References


Fox MD, Raichle ME (2007) Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat Rev Neurosci 8:700-711.


