

Chapter 2

The Neurology of Creativity: Focus on Music

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Abstract Creativity has been a very difficult human quality to study, but is now beginning to be understood at the neurobiological level. The most recent theories suggest that the major lobes of the brain, in particular interactions between the frontal lobes and temporal lobes, are critical for maximizing the potential for creative endeavors. The neural circuitry of the limbic system, as well as catecholaminergic neurotransmitter pathways and their lobar interactions, is also important in the process. Music is one of the most creative and complex of all human activities and appears to involve numerous regions and pathways within the brain. The process of listening to music involves many specialized regions, including the auditory pathways, Heschl's gyrus, the planum temporale (PT), and auditory association areas. Musical performance involves coordination between the neuromuscular system while playing an instrument, with simultaneous and constant auditory feedback on the quality of the performance and the need for any necessary adjustments. The process of music perception while listening or performing requires acoustical analysis of pitch, melody, and harmony, the use of auditory memories, analysis of musical syntax and emotional responses, and many other functions, all performed over a matter of milliseconds in the dedicated musical neural networks in the brain. In addition, the brains of musicians and non-musicians are now known to be different, with musicians having specialized networks and connections as a result of formal musical training. The origins of music, as well as the anatomical and neurobiological underpinnings of musical perception, performance, and training, are reviewed in detail.

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2.1 Creativity: Definitions and Overview

For hundreds of years, the underpinnings of human creativity have been debated by philosophers, psychologists, neurologists, psychiatrists, and cognitive neuroscientists. To this day, a complete understanding of this complex and mysterious process remains elusive (Hennessey and Amabile 2010). Creativity has been very difficult to study in human subjects and, due to its abstract nature, has been very difficult to translate into plausible animal models. Although there have been numerous attempts at defining creativity, all of them fall short of describing the process as it applies across all disciplines, including basic science (e.g., physics, chemistry), medicine, architecture, art in all of its forms (e.g., painting, sculpture, drawing), music, literature, and film. From a broad, cultural point of view, a creative idea or activity can be defined as a concept or formulation that is both novel and useful (or influential) in a particular social setting (Hennessey and Amabile 2010; Perkins 1988). This definition allows for the “cultural relativity” of many creative ideas or activities, since some might be considered novel and brilliant in a primitive or backward society, but might not be considered so creative or important in a more advanced culture. In addition, it helps make the distinction between the truly creative individual and others that are merely eccentric or have aspects of mental illness. Although there is a correlation between creativity and some aspects of psychopathology (e.g., anxiety, depression, hypomania; discussed in more detail below), it is not associated with “full-blown” mental illness, such as schizophrenia, mania, or melancholic depression. Another definition of creativity, with applications to more scientific endeavors, has been postulated by Heilman (2005) in his book *Creativity and the Brain* and states that creativity is “the ability to understand, develop, and express in a systematic fashion novel orderly relationships” (Heilman 2005). This definition is very helpful in understanding the creative process in the scientific disciplines (e.g., physics, chemistry, medicine), where the creative mind is trying to explain new anomalous findings that do not fit in with the current paradigm, but has limited value when applied to more artistic pursuits such as painting or writing music.

Earlier neuroscientific concepts of creativity from the 1970s were dominated by the theory of “hemispheric specialization,” in which the non-dominant hemisphere (typically the right hemisphere) was considered to be specialized for creative activity in all disciplines, as well as holistic pattern recognition (Hennessey and Amabile 2010; Hoppe 1988). This theory was developed out of neuropsychological study of patients after corpus callosum transection surgery for intractable epilepsy. However, the lateralization model applies poorly to language-based creative activities, since language is supposed to be mediated in the dominant hemisphere. In addition, later evidence suggested that maximizing the function of both hemispheres was more important for creativity than selectively activating the right hemisphere (Martindale 1999). Moreover, further brain lesion studies noted that

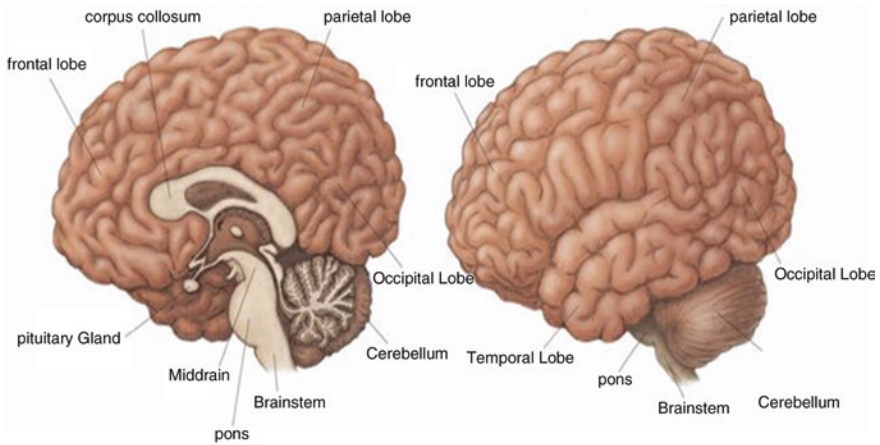


Fig. 2.1 Diagrams showing the medial and lateral surfaces of the brain, including the major lobes: frontal, parietal, temporal, and occipital, along with the cerebellum and brainstem

right or left hemispheric damage rarely affected creativity selectively. This is all consistent with a recent meta-analysis of hemispheric specialization and creativity, which did not find a predilection for right hemisphere activation during creative thinking and related activities (Mihov et al. 2010).

More modern theories on the neurobiology of creativity focus on lobar functions and lobar connectivity, in particular the interactions between the frontal lobes and portions of the temporal and parietal lobes (see Fig. 2.1) (Hennessey and Amabile 2010; Heilman et al. 2003; Flaherty 2005; Shamay-Tsoory et al. 2011; Abraham et al. 2012). Recent research has also implicated the limbic system, with its innate drive for human interaction and communication, as playing a role in creativity. Integral to connectivity between the different lobar areas, as well as for limbic system input into the frontal lobes, are the various catecholamine neurotransmitters expressed in neurons of these different neural networks. In particular, it is now becoming apparent that the degree of dopaminergic and noradrenergic activity, mainly from limbic and locus coeruleus projections into the major lobes, is also important for the creative process. In the following sections, we will review in more detail the various components of the lobar theory of creativity.

2.1.1 The Temporal Lobes and Creativity

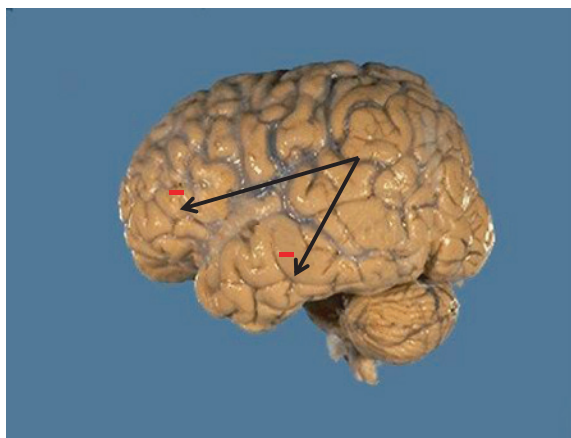
Early on in the development of the lobar theory of creativity, it was postulated that the temporal lobe might be the neuroanatomical location for creative drive. This was based on the fact that hypergraphia, a compulsive drive to write, was localized to the temporal lobe in some patients with temporal lobe epilepsy, typically on the right side (Yamadori et al. 1986). Hypergraphia was considered a by-product of an

overall decrease in temporal lobe activity. However, hypergraphia is even more commonly diagnosed in patients with mania and related states of hyperarousal. In patients with a mild form of mania and hypergraphia, there can be a high degree of creativity and novel idea formation. SPECT imaging studies in manic patients have shown an increase in activity in the right anterior temporal region, while EEG studies have shown a decrease in lower left temporal quantitative activity (Flaherty 2005). Mania is most likely to occur secondary to temporal lobe lesions on the right side, although other lobar brain lesions have been implicated (Braun et al. 1999). Frontal lobe lesions can occasionally induce mania and pseudomania, but typically show dysfunction of the temporal lobes as well on PET imaging. Although the correlation between manic states and creativity is most powerful for language-based fields, temporal lobe dysfunction can also result in the equivalent to hypergraphia in other creative endeavors.

For example, in some patients with frontotemporal dementia, a progressive neurodegenerative condition that results in frontal lobe and temporal lobe atrophy, there is a subset of patients (approximately 5–10 %) with predominantly temporal lobe damage that can develop compulsive artistic or musical interests (Flaherty 2005; Miller et al. 1998). Some of the patients developed these compulsive interests even in the absence of any prior artistic or musical tendencies. Damage to the superior, posterior dominant temporal lobe (usually left sided) near Wernicke's area can result in a receptive or Wernicke's dysphasia, in which the patient has increased speech output, along with impaired comprehension. Typically, the patient is unaware of the errors in the content of their speech. Non-dominant temporal lobe lesions do not impair comprehension, but are often associated with hyperverbosity and pressured speech, and may disinhibit left hemisphere language function (Braun et al. 2004).

Can the temporal lobes be assigned the site of creativity in the brain? Based on the information cited above, it is unlikely that creativity is mediated in the temporal lobes. Furthermore, since we know that the vast majority of temporal lobe efferents are inhibitory, it might be more accurate to say that the temporal lobes are the “region of creative suppression.” For example, there are large temporal lobe efferent fiber bundles that inhibit the frontal lobes (see Fig. 2.2). And, most of

Fig. 2.2 Lateral surface of the brain, showing the frontal lobe and temporal lobe, with the inhibitory cortico-cortico connections in place, which are mutually inhibitory (see text for more details)



the above-mentioned conditions that were known to trigger creativity or creative drive (e.g., psychiatric conditions, neurodegenerative disorders) were doing so in the context of some form of disruption to normal temporal lobe function.

2.1.2 The Frontal Lobes and Creativity

In the lobar theory of creativity, the frontal lobes are hypothesized to play a more central role in the creative process. However, for many individuals, the frontal lobes are implicated in the setting of “creative block,” when there is some form of frontal lobe dysfunction associated with an illness that is disrupting creative expression (Hennessey and Amabile 2010; Heilman 2005; Flaherty 2005). In general, a lack or loss of creative drive is much more common than an excessive creative drive. There is a strong correlation between creative block and frontal lobe malfunction from numerous conditions, including depression, anxiety, Broca’s aphasia, abulic mutism, tumors, and strokes. The most common condition to result in creative block and frontal lobe dysfunction is depression. In the depressive state, there is a loss of motivation and cognitive flexibility, loss of interest in eating and sex (i.e., generalized anhedonia), and a loss of creativity. Imaging and functional studies are very consistent in demonstrating reduced or abnormal frontal lobe function, including functional MRI (fMRI), PET, SPECT, and MR spectroscopy (MRS) (Heilman 2005; Flaherty 2005; Liotti and Mayberg 2001; Wang et al. 2012; Liu et al. 2012). Once the depression has been successfully treated (e.g., anti-depressant medication, psychotherapy), frontal lobe function returns to baseline over time (Goldapple et al. 2004).

When the depressive episode has improved enough for motivation to normalize, there can be a reversal of creative block. Stimulant medication can also be helpful in treating depressive symptoms, including creative block (Flaherty 2005). Anxiety disorders, alone or in combination with depression, can also lead to frontal lobe dysfunction and contribute to creative block (Cannistraro and Rauch 2003). Recent studies show that anxiety can modulate hypoactivation in the middle frontal lobe and insular regions of the brain (Schlund et al. 2012). In this context, the creative block is similar to “performance anxiety” and is associated with a high degree of emotional arousal. Treatment of the anxiety (e.g., anxiolytics, anti-depressants, psychotherapy) should result in a reduced level of emotional arousal and improvement in creative block. Another frontal lobe condition with similarities to creative block, in particular writer’s block, is Broca’s dysphasia, secondary to damage in and around the pars opercularis region of the inferior frontal lobe (i.e., anterior speech area) (Heilman 2005; Flaherty 2005). Broca’s dysphasia causes a selective deficit in speech production and fluency (including written language), along with a variable degree of word finding difficulty (i.e., dysnomia). Patients with Broca’s dysphasia are very aware of their language deficits and speech errors and tend to be very frustrated and depressed by their limitations and reduced linguistic output.

A similar kind of frustration, anger, and depressed mood can be seen in patients with severe or prolonged writer’s block. Lesions or damage within the frontal

lobes outside of Broca's area can also cause depression and diminished speech output, along with other symptoms such as cognitive deficits, abulia or a lack of emotion, loss of motivation, and perseveration. Creative block can also be noted in patients with this kind of frontal lobe damage. The medial prefrontal cortical region appears to be very important for motivation and creativity, because damage to this area (e.g., brain tumor, stroke, hemorrhage, degenerative disease) can lead to amotivational, abulic states of decreased creative drive. For example, in a study of the frontal variant of frontotemporal lobar degeneration (fvFTLD), patients with the disease were compared to non-demented Parkinson's disease patients and normal healthy controls on a standardized test of creativity, as well as on tests of frontal lobe function (de Souza et al. 2010). The patients with fvFTLD were strongly impaired in all dimensions of the Torrance Test of Creative Thinking, in comparison with parkinsonian patients and controls. Poor creativity was strongly correlated with frontal lobe testing abnormalities and prefrontal hypoperfusion. The dorsolateral prefrontal cortex does not appear to be as important for creative drive and is more involved in working memory and flexible problem-solving abilities that can be applied to creative skills.

Normal frontal lobe function appears to be necessary for creative activity, but there are qualitative and quantitative differences between individuals in terms of how well the frontal lobes perform. In a study of regional cerebral blood flow (rCBF) in a matched set of healthy male subjects who scored either very high or low on a standardized creativity test, the baseline level of frontal lobe activity was higher in the creative group (Carlsson et al. 2000). In addition, there was a greater percentage of frontal increase in rCBF while performing creative tasks in the high creativity group. Overall, there was more activation (i.e., increased rCBF) in the bilateral prefrontal regions, left temporal lobes, and right cerebellum in the creative subjects. Transcranial electromagnetic stimulation (TMS) of the major lobes or deep brain regions is a noninvasive method with the ability to increase the activity in large groups of neurons (Hampson and Hoffman 2010). Preliminary studies have suggested that TMS over the frontal lobes can increase creativity in normal subjects when they are performing drawing and writing tasks (Snyder et al. 2004). Similarly, there are case report studies of patients that have had increases in creativity after undergoing subcortical deep brain stimulation with electrodes near the nucleus accumbens, a deep nucleus in the ventral striatum (Gabiëls et al. 2003; Flaherty et al. 2005). This is most likely related to connections between the nucleus accumbens and the frontal lobes, temporal lobes, and limbic system, and its supportive role in the generation of limbic drives.

Finally, it must be emphasized that the creative process often involves perseverance and persistence, independent of the domain in which the individual is creatively active (Heilman 2005). Goal-oriented behavior and persistence of activity are primarily mediated by the intact frontal lobes. Proper function of the frontal lobes allows the individual to plan and implement goal-oriented behaviors, but also inhibits and controls the more phylogenetically primitive neural systems, such as the limbic system. Inhibition of primitive biological drives and emotions is critical for goal-oriented and societally relevant behaviors, including creative endeavors.

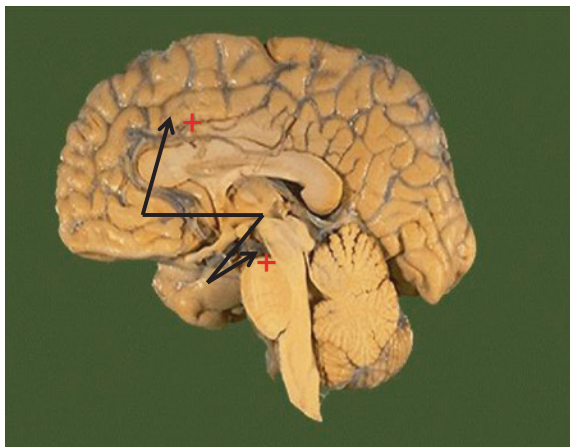
2.1.3 *IQ, Neurotransmitters, Limbic System, and Creativity*

Early studies on the relationship between IQ and creativity demonstrated that they were only moderately related and that a person's IQ could not always predict their creative capacity (Heilman 2005; Torrance 1975). For example, when subjects with low IQs were tested for creativity, they consistently scored poorly. However, when subjects with high IQs were tested, there was a variable correlation with creativity. Another study looked at the relationship between the IQ and creative abilities of architects and found a poor correlation (Barron and Harrington 1981). It was concluded that for subjects with an IQ of 115–120 or higher, the IQ was not able to predict creativity as much as it does when the IQ is below 115. Therefore, there appears to be a threshold effect with IQ, and a person's IQ needs to be above a certain level in order to have sufficient intelligence to learn the knowledge set and acquire the skill sets that are necessary to be creative in a specific domain. Thus, intelligence is a necessary component of creativity, but once an IQ of 115–120 is reached, the motivation of the subject becomes the dominant feature that will drive creativity (Sternberg and O'Hara 1999). If a group of individuals with high IQs are all asked to develop creative ideas, the more highly motivated in the group will cultivate a larger number of ideas. Through the laws of Gaussian statistics, this will more likely result in a proportionately higher number of ideas that are novel and unique.

The neuroanatomical correlates of IQ and creativity remain elusive, but do seem to involve “connectivity” between nerves in the brain, as well as between different regions of the brain (Heilman 2005). Animal studies have demonstrated that the thickness of the cerebral cortex and the density of dendritic spines on cortical neurons are important for intelligence and performance (Rosenzweig and Bennett 1996). This type of augmented connectivity is seen in animals after being raised in “enriched environments.” Having cortical neurons with amplified connectivity could increase the potential for more widespread neuronal networks necessary for faster learning and a greater capacity for knowledge. Enhanced connectivity between different regions of the brain is also thought to be involved in more creative individuals—between the right and left hemispheres, as well as between the major lobes, especially portions of the frontal, temporal, and parietal lobes. More widespread and enhanced neural connectivity would allow the creative individual to combine informational stores and representations of ideas in novel ways that were heretofore impossible.

It is well known that creative people have higher baseline levels of arousal and greater responses to sensory stimulation (Martindale 1999). Dopamine activity is known to decrease latent inhibition—which is a behavioral index of the ability to habituate to sensations (Swerdlow et al. 2003). Low latent inhibition can sometimes overload an organism with stimuli and is seen in various psychotic states. However, low latent inhibition is also a characteristic feature of creative individuals with high intelligence (Carson et al. 2003). The difference between the person with psychosis and the highly intelligent and creative individual is the ability to find patterns and order in the flood of sensory data, so it is less chaotic and disorienting. In addition to increasing baseline levels of arousal, dopamine activity can also induce focused creative arousal, which is highly goal-directed, and may be driven by

Fig. 2.3 Mid-sagittal view of the brain, showing the mesolimbic dopaminergic projections to the frontal and temporal lobes. These pathways facilitate the creative process by reducing latent inhibition (see text for more details)



mesolimbic dopaminergic efferents (see Fig. 2.3). Dopamine is also known to mediate reward-seeking behaviors such as gambling and cocaine addiction, as well as the appreciation for music and beautiful faces, and the need to communicate (Heilman 2005; Aharon et al. 2001). However, an excess of dopaminergic activity (e.g., L-dopa, dopamine agonists) can have deleterious consequences, including stuttering, coprolalia, hypomania, hallucinations, dystonias, and highly complex repetitive and stereotypical behaviors (e.g., assembling and reassembling an engine) (O’Sullivan et al. 2009). In contrast, dopamine antagonists, which are often used as anti-psychotic agents, are able to suppress hallucinations and stereotypical behaviors, as well as the free associations that are helpful in creative activity. One possible mechanism for the ability of dopamine to mediate focused reward-seeking behavior is a center-surround inhibition model (Mink 1996). In this model, dopamine is able to facilitate voluntary, goal-directed activity while simultaneously inhibiting competing behaviors and activities. This model has been well established in many motor and sensory systems within the brain, including the basal ganglia, retina, and visual processing centers. Dopamine may also play a role in creative discovery through its effect on novelty-seeking behavior, in particular through allelic variations of the D4 receptor (Keltikangas-Jarvinen et al. 2003).

The temporal lobes are thought to play a role in mediating the interactions between limbic dopaminergic activity, novel creative thought, and novel thoughts that are actually psychotic. For example, functional MRI studies have shown that schizophrenic auditory hallucinations—which can resemble a creative idea—selectively activate the temporal lobe (Shergill et al. 2001). In addition, metaphoric, cross-modal thoughts, and concepts are selectively impaired by temporal lobe dysfunction and damage (Jakobson and Halle 2002). Metaphoric thoughts and concept formation are critical for creative endeavors, since they depend on being able to detect analogies and relationships between phenomena that were previously thought to be unrelated. When metaphoric thoughts become extreme, they can pass into the psychotic spectrum toward delusional thought processes.

Many creative scientists, artists, and musicians claim to be most productive when they are in a relaxed, unstressed, and peaceful state of wakefulness. At these moments, the levels of brain and circulating catecholamines, in particular norepinephrine, are at reduced levels, which may be important for maximizing the size and connectivity of available neural networks (Heilman 2005; Heilman et al. 2003). As mentioned before, creativity and novel concept formation will be most robust when the number of neural networks, and connectivity between the networks is at its peak. With higher levels of norepinephrine and cortical arousal, the associative field of neural networks and their connectivity is suppressed, thereby limiting creative potential. This process is likely mediated through the noradrenergic projections from the locus coeruleus in the brainstem to the frontal lobes and inferior parietal lobes (Morrison and Foote 1986). The negative effect of catecholamines on the size of neural networks and cognitive flexibility has been studied and verified in animal models and human subjects (Heilman et al. 2003; Beversdorf et al. 1999).

2.1.4 Neurobiological Model of Creativity and Summary

A useful model that graphically represents many aspects of the lobar theory of creativity has been proposed by Dr. Alice Flaherty, a Neurologist at the Massachusetts General Hospital and Harvard Medical School (see Fig. 2.4) (Flaherty 2005). In this model, the y-axis is a continuum of dopaminergic activity that at the low end demonstrates slow action, emotion, and thought processes, and at the high end represents goal-directed and creative behavior. The x-axis is a continuum of lobar activity, showing normal frontal and temporal lobe activity in the middle, with abnormal frontal lobe activity toward the left and abnormal temporal lobe activity toward the right. If you move from the “Normal” region up the x- and y-axes (i.e., toward the hypothetical “zero”), you initially enter into a region of creative block, with mild frontal lobe dysfunction and reduced dopaminergic activity. The individual would experience a loss of creative ideas and novel concept formation, but would still be able to function in other spheres of activity. As you continue to move further up the axes, you pass this region and enter into a more severe state of profound frontal lobe dysfunction and loss of dopaminergic activity, and begin to display severe depression and/or abulia, with slowing of mentation, movement, and activity. Moving from the “Normal” region down the x- and y-axes, you initially enter a region of creative drive, with mild temporal lobe dysfunction and higher dopaminergic activity. The individual would experience improved creativity and idea formation, with otherwise intact function in other spheres. However, with this alteration of temporal lobe function, you would also be at higher risk for mild psychopathology, similar to many artists and writers (e.g., depression, bipolar disease, anxiety disorder). As you continue to move down the axes, you pass the Creative Drive region and enter into a state of severe temporal lobe dysfunction that, even with the higher level of dopaminergic activity, results in psychiatric impairment in the form of mania and psychosis. The model is not complete yet and would be more accurate if it was 3-dimensional,

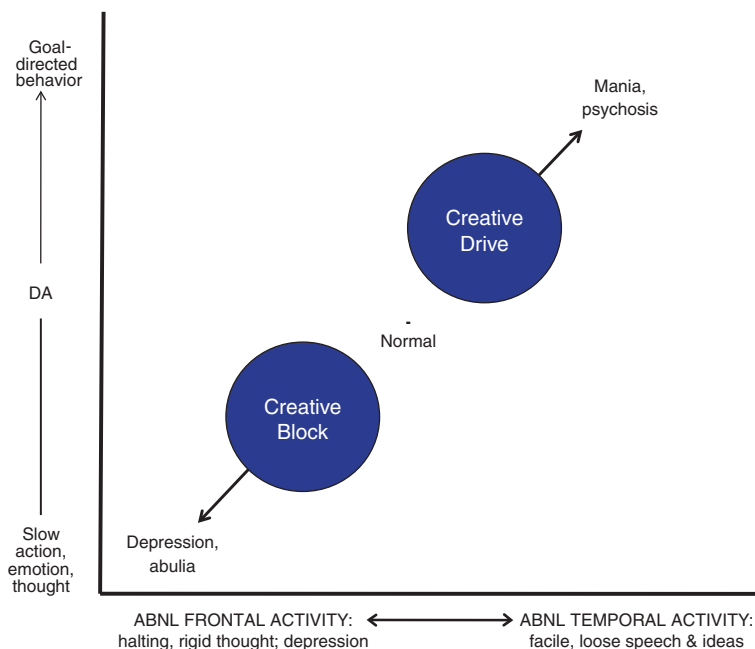


Fig. 2.4 Neurobiological model of creativity proposed by Dr. Alice Flaherty. The *y-axis* shows the continuum of dopaminergic activity, with higher levels being more inductive to creative activity. The *x-axis* shows the continuum of frontal lobe and temporal lobe activity, with the most creative combination requiring at least some degree of temporal lobe dysfunction. Adapted from Flaherty (2005), with permission from the author

so that frontal lobe function and temporal lobe function could vary independently (Flaherty 2005). In addition, it would allow for more accuracy if the lobar subsystems could also be incorporated into the model: frontal (orbitofrontal, dorsolateral, medial frontal) and temporal (lateral and medial).

In summary, creative drive will increase with mild-to-mild/moderate degrees of temporal lobe dysfunction in combination with increasing dopaminergic tone. Creative block increases with reduced or altered frontal lobe function in combination with decreasing dopaminergic tone.

2.2 Neurology of Music: Definitions, Overview, and Origins

Music is one of the most creative and complex of human endeavors, yet remains difficult to define since it can be described in many contexts, including that of musical listener, musician, social lubricant for various types of functions (e.g., religious, entertainment, educational, familial, medical, political), sociological,

and evolutionary (Cross 2001; Huron 2001; Fitch 2006; Peretz 2006). One definition that has been offered by Cross states that music can be conceived of as individual abilities to process and respond to sonic patterns that are constituted by complex pitch and rhythmic structures (Cross 2001). This definition is very limited, is most accurate in the setting of the passive listener (e.g., an individual at a musical concert), and is less helpful for more social applications of music where it is used as an interactive medium in a group setting, or in explaining the individual who is driven to write and play music.

A broader definition of music proposed by Sessions suggests that music is sound that is organized according to principles of pitch, rhythm, and harmony, with musical timbres that allow for the differentiation between musical sound sources and musical instruments (Sessions 1950). No matter how it is defined; however, music has been an integral aspect of the human experience for millennia. Indeed, there is a consistent record for the presence of music making in human settlements from all over the world. Archeological evidence (e.g., prehistoric bone flutes) suggests that instrumental music has been present within human cultures for at least 40,000 years, and perhaps much longer (Huron 2001; Fitch 2006). There is also a controversial bone flute (made from a cave bear bone) from a Neanderthal burial site that has been dated to approximately 43,000 years ago (Kunej and Turk 2000). If this bone flute is legitimate, it would suggest that instrumental music has origins in the common ancestor of Neanderthals and *Homo sapiens*—*Homo heidelbergensis*—dating back more than 500,000 years ago (Tattersall and Schwartz 2009). However, critics of this research have suggested that the artifact was not a flute, but instead an ordinary bone that had puncture marks from the teeth of a predator. Nonetheless, the presence of human bone flutes from 40,000 years ago implies that the use of flutes and other instruments made from easier to manipulate and less well-preserved materials, such as reeds, wood, and sticks, would likely predate them by thousands of years (Huron 2001; Fitch 2006). It is also very likely that the use of rattles, shakers, and drums predate the use of bone flutes, which are somewhat complicated, by many thousands of years (some authors estimate by another 50,000 years), since they are ubiquitous instruments in hunter-gatherer societies from all over the world (e.g., American Indians, African tribes, Polynesian tribes). Furthermore, many authors also assume that vocalizations, or some type of crude singing, were the first form of music ever produced by individual humans (e.g., mothers singing to infants) and within human societies (e.g., singing as ritual in religious ceremonies or in preparation for battle). Singing as a form of music is estimated to predate instrumental music by 50,000–150,000 years using conservative estimates, and even longer by those researchers who feel that human song evolved before or simultaneously with speech (see discussion below). Based on the data above, it can be estimated that human music making came into existence from 100,000–250,000 years ago, and possibly much longer.

The long-standing history of music has led to many theories about potential evolutionary aspects of music, and how it might have evolved within the human brain in a similar fashion to language. Language is a universal human characteristic—all humans are able to acquire language, unless they are suffering from a

pathological condition or severe social deprivation. The acquisition of language requires exposure to, and engagement in, linguistic interactions within a time-sensitive period, generally considered to be from just after birth until approximately 4–5 years of age. The use of language is a specifically human ability, since it is not acquired spontaneously in any other species and only in rudimentary fashion by our closest primate relatives (Pinker and Jackendoff 2005). There are also very specialized regions of the brain that mediate language function, mainly lateralized to the left hemisphere and involving networks that incorporate Broca's area in the inferior frontal lobe (Brodmann area 44) and Wernicke's area (Brodmann areas 21 and 42) in the inferior parietal lobule.

The structural and linguistic aspects of language are universal (e.g., phonology, morphology, syntax, and semantics) and transcend all cultural, social, and societal barriers. It is also clear that the acquisition of language provided powerful evolutionary advantages for humans, in terms of increasing their ability to communicate to one another and develop large and complex social structures, all of which would have significant survival value. There are clear similarities between language and music, such as the presence of a hierarchical structure (syntax vs. harmony), a vocabulary (words vs. chords and intervals), tonal properties (inflection vs. timbre), and temporal features (prosody vs. rhythm). However, despite the substantial overlap between the neurobiological “design features” of music and language, there are also important differences. For example, language is able to “convey an unlimited number of propositional thoughts or ‘meanings’ with arbitrary specificity,” while music is more limited (Fitch 2006). In addition, the ability to play music (or sing) does not have a “critical” or time-sensitive period similar to that of language acquisition, although it is true that most professional musicians started playing while very young (i.e., typically before 8 years of age). However, it is still possible to become quite proficient at playing instrumental music, even when the initial learning and “skill acquisition” do not occur until the teenage or adult years. Furthermore, music does not have the same body of structural comparative data, or cross-cultural and cross-societal universality, as that of language. Anatomically, there are no regions of the brain specifically evolved to mediate critical musical functions, as there are for the production and processing of language (i.e., Broca's, Wernicke's). As we will discuss later, the neurological processing of music is much more diffuse and involves numerous regions within the right and left hemispheres of the brain.

In spite of the differences noted above, is it possible that music, in the form of primitive or crude vocalizations and song, could have predated spoken language in humans and been an evolutionary predecessor? Indeed, this theory has been proposed by numerous investigators, including Darwin and Livingstone (Huron 2001; Fitch 2006). In the late 1800s, Darwin suggested that a primitive song-like communication system may have been a precursor to human language and been adaptive for the “progenitors of man,” so that modern music might be a behavioral fossil derived from this past system (Darwin 1871). Based on this hypothesis, humans would have passed through at least one prelinguistic communication system or “proto-language” since our split with chimpanzees and before attaining full

modern language (Arbib 2005; Masataka 2009). Over the course of this 5–6 million years of evolution, different selective pressures and forces would have driven different components of modern language capacity.

The hypothesis of a shared ancestral precursor of music and language is quite parsimonious, in that it recognizes many shared features of language and music, while allowing for the evolution of their differences, in particular the development of semantics in language, in a straightforward phylogenetic sequence. It is also consistent with the greater individual variability in music-making skills of modern humans (which are no longer strongly selected) in comparison with language skills (which are still under powerful positive selective pressure) (Judd 1988). In the field of comparative biology, there is strong evidence that music-like communication systems can evolve relatively easily (e.g., three different types of bird songs in birds, whale song, great ape drumming), while a complex communication system that allows for the ability to convey arbitrary meanings has evolved only once, in the form of human language (Fitch 2006). Therefore, a hypothesis that proposes that complex vocal signals (i.e., song) evolved first, followed by the attachment of meanings to those signals at a later time, are quite elegant and consistent from a comparative viewpoint (Fitch 2005). If the musical proto-language hypothesis is valid, then questions regarding the modern utility or purpose of music are moot. According to this hypothesis, proto-music might once have had specific functions (e.g., courtship, territoriality), but in the modern era exists only as a remnant, with its critical functionality replaced by the use of language.

In addition to an evolutionary process in which music (in the form of primitive vocalizations and song) might have evolved as a precursor to spoken language, what other evolutionary pathways have been proposed and discussed as possible evolutionary origins of music (Cross 2001; Huron 2001; Fitch 2006; Peretz 2006)? Several broad categories have been proposed, including *mate selection*, *social cohesion*, *group effort*, *perceptual development*, *motor skill development*, *conflict reduction*, *safe time passing*, and *transgenerational communication* (Huron 2001). *Mate selection* refers to the possibility that music making may have arisen as a courtship behavior and improved the ability to attract a good partner. *Social cohesion* refers to the ability of music to contribute to group solidarity, promote altruism within the group, and increase the effectiveness of collective action (e.g., hunting, defense). *Group effort* refers to the ability of music to contribute to the coordination of group work, such as the creation of living quarters or building a ship. *Perceptual development* refers to the idea that listening to music might provide an “exercise” for hearing and might improve the perceptive abilities of individuals in the group. *Motor skill development* refers to the ability of making music (especially instrumental music) to improve and refine motor skills. *Conflict reduction* refers to the possibility that the use of music in social situations might have led to a more relaxed environment, with less interpersonal conflict. *Safe time passing* refers to the possibility that playing music or listening to music might have provided a benign form of time passing, as human social groups became more efficient at gathering food and had more free time. *Transgenerational communication* refers to the ability of music (e.g., folk songs) to convey socially relevant history and other information over long periods of time.

Of many theories noted above, the ones that suggest an important role for music in the larger sphere of social interaction are likely to be the most significant (Huron 2001; Fitch 2006). Music is a very powerful means to establish behavioral coherency in large masses of people, which could easily have had survival value in the more primitive past (Roederer 1984). In addition, music might have originated as a means for large-scale social bonding, with the ability to synchronize the mood of many individuals in a large group, thereby preparing the group to act in unison to accomplish socially relevant goals. The mood synchronization effect of music could serve many socially important functions that would have evolutionary implications, such as having a calming effect in the setting of social gatherings where group harmony and bonding were important (e.g., wedding, funeral), or in raising spirits and aggression levels in preparation for a war party or to protect home turf against warring tribes. In these situations, music is playing a social role in its ability to help define a sense of group identity and common purpose, by synchronizing individual moods to serve the larger goals of the group. Along these same lines, recent work by Fukui and others has shown that listening to highly favored music can lead to a lowering of testosterone levels in males (Fukui and Yamashita 2003).

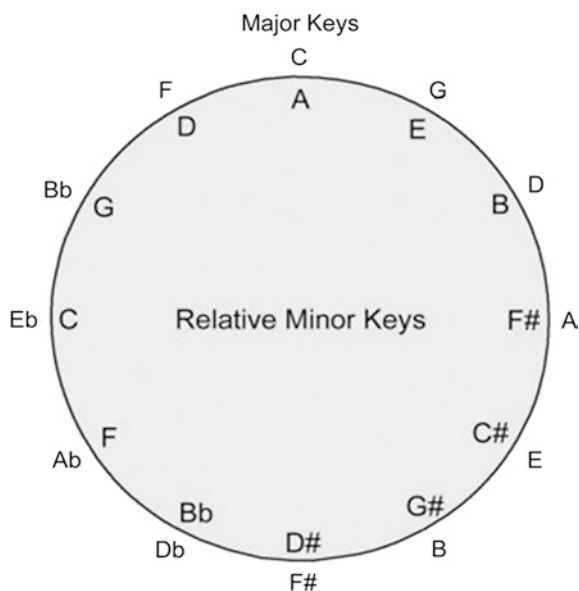
This finding has social and evolutionary significance, in that lowering of testosterone levels would likely result in less aggression, less conflict, less sexual confrontation, and less sexual competition, thereby engendering more group cohesion. Similarly, it has been suggested by Freeman and others that listening to music can induce the release of oxytocin in the brain (Huron 2001; Freeman 1995). It is known that oxytocin is important for pairing life events with strong memories, especially those involved with major limbic activation, such as trauma, sexual activity and orgasm, ecstasy, and strong emotional arousal. In addition, the release of oxytocin has been correlated with human and animal bonding circumstances, such as mate-bonding, mother–child bonding, and general social bonding. Therefore, the release of oxytocin while listening to music has important implications for individual-to-individual bonding, peer-group bonding, and the development of a social identity in many settings, such as courting lovers, religious groups, college students and alumni groups, business groups, and military organizations.

2.2.1 Musical Structure and Music Theory, Neurobiology of Musical Listening

Music is composed of individual notes, with each note corresponding to a different pitch or frequency (Surmani et al. 2004). In general, the higher the perceived pitch of a given note, the higher will be the frequency of the associated vibration; similarly, the lower the perceived pitch of a note, the lower the frequency. There are seven basic notes, including A, B, C, D, E, F, and G, along with their corresponding sharps and flats. These notes can be arranged into various chords and scales (e.g., major, minor, pentatonic) built around each of the root notes and form the backbone of the structure of music. In Western music, there are 12 different notes that represent the

Fig. 2.5 The *Circle of fifths*.

The diagram demonstrates the relationships between musical keys. The major keys are shown on the *outside of the circle*, while the minor keys are shown on the *inside of the circle*. As one progresses along the *circle of fifths* from the major key of C, there is a systematic change in the number of sharps or flats associated with each key. Adapted from Hetland (2000), with permission from the author



roots of the major and minor keys, as shown in the Circle of Fifths: C, G, D, A, E, B, F#, Db, Ab, Eb, Bb, and F (see Fig. 2.5). The circle of fifths is a visual representation of the 12 tones of the chromatic scale, along with their corresponding key signatures and associated major and minor keys. The circle is very helpful for musicians and composers while composing and harmonizing melodies, building chords, and moving to different keys within a composition (Surmani et al. 2004).

Once a musical composition is complete, whether the genre is rock, classical, jazz, or pop, it will have numerous features that can be broken down into basic components that are all processed simultaneously in the brain during the listening process. These features of music include basic pitch, pitch contour, melody, harmony, timbre, form, dynamics, duration, articulation, temporal structure (rhythm, meter, beat, tempo), consonance and dissonance, loudness, and emotional responses. As mentioned above, *pitch* is the perceived sensation of the frequency of a given note in a piece of music, with different notes being relatively higher or lower in pitch to one another. Most people have relative pitch, with the ability to perceive basic differences in pitch interval or frequency (i.e., higher or lower) between two notes or a series of notes. Perfect or absolute pitch is the ability to identify, after hearing a random musical note without comparison with other notes, its exact pitch (e.g., middle C). Perfect pitch is uncommon, with an estimated incidence of 1 in 10,000 individuals (Ross et al. 2005). The difference in frequency between two pitches is called an interval, with the common intervals being thirds and fifths, from the root pitch or note. It is common in Western music to form larger pitch structures called chords, which contain more than two pitches. The most basic type of chords begin with the root pitch or root note in the lowest position and then add in a note that is a third above the root, followed by a note that is a fifth above

the root (or another third above the second note in the chord; e.g., C major chord: C-E-G). *Pitch contour* refers to the relative change in pitch over time of a primary sequence of notes in a piece of music (i.e., the “ups” and “downs” in the song).

The pitch contour (or “envelope” of pitches around the core notes of the music) can vary widely between songs and types of music (e.g., a simple folk song vs. a robust classical composition). The *melody* of a piece of music consists of the linear succession of pitches or notes (i.e., the “horizontal” aspect of music) that the listener perceives as a single musical phrase or entity that is the centerpiece of the song. Melodies often consist of one or more musical phrases or motifs and are typically repeated throughout the composition in various forms. The core of a given melody is usually created with the use of chord progressions, scales, or modes. In Western classical music, an initial melody or theme is usually introduced and then followed by variations on the primary melody. In jazz, the “lead” or main melody is used as a starting point to begin the song, followed by improvisation into secondary or counterpoint melodies. In rock, folk, and pop music, there are usually two related melodies (i.e., verse and chorus) that are used throughout the song, with possible variations in the phrasing and lyrics within each component. *Harmony* within a musical piece refers to the use of simultaneous pitches or notes that can be provided by the use of chords, multiple instruments, multiple voices, or a mixture thereof.

In contrast to melody, harmony is considered the “vertical” aspect of music and involves chords, chord construction, and chord progressions. In Western music, most harmonies are tertian, with the pitch intervals based on thirds (e.g., root, third, fifth, seventh), giving a consonant or pleasing sound. In some forms of music (e.g., jazz), the harmonic structures may be different, using chords and chord progressions that have more dissonant qualities. The temporal structure of a musical piece has several components, including the *rhythm*, *meter*, *beat*, and *tempo*. The *rhythm* of a song consists of the arrangement or pattern of sounds (i.e., pitches, notes) and silences over time and is often consistent throughout a given melody. In Western music, the rhythm of a song is usually arranged with respect to a time signature or *meter*, in which a measure is defined as having a certain number of beats (e.g., 2/4 time, 4/4 time). The *beat* of the music is the underlying periodic pulse or tactus of a composition (e.g., the beat of the bass drum in rock music) that induces listeners to entrain as they tap their feet with the song. The *tempo* of a song is the speed or frequency of the beat and is usually measured in “beats per minute” or bpm. The tempo can differ significantly between various styles of music, ranging from 40 bpm to over 200 bpm. *Timbre*, also known as tone color or tone quality, refers to the unique characteristics of a given note or sound and allows us to perceive the differences between different voices, as well as between various musical instruments, such as string instruments, wind instruments, horns, and percussion instruments. For example, if an electric guitar, piano, and French horn are all playing the same note (e.g., middle C) at the same loudness, they are easily differentiated from each other based on characteristics of timbre and sound quality. Some of the terms used to analyze the differences in timbre between different musical instruments include harmonics, spectral envelope, time envelope, brightness, warmth, and tonal character.

Harmonics refer to the frequencies of sound that are produced by a given instrument that may be above or below the fundamental frequency (e.g., middle C) being played, and in many cases will be both. The spectral and time envelope of a given instrument refers to several qualities of its sound, such as attack time, attack characteristics, decay, sustain, and release (i.e., the ADSR envelope). The envelope is the overall amplitude structure of a sound, which is unique between different voices and different instruments. Musical *dynamics* refers to the softness or loudness of a note or musical phrase (e.g., pianissimo, fortissimo), while musical *articulation* describes the specific techniques used to execute or play the notes or phrases (e.g., staccato, legato). Musical *consonance* and *dissonance* generally refer to the quality of chord and harmonic structures, and whether they are complementary and pleasing to the ear or not. Consonant chords and harmonies have pitch intervals that are complementary (e.g., octaves, thirds, fifths) and increase each other's resonance, and are generally considered to be pleasant to the listener. In contrast, dissonant chords and harmonies have intervals that are considered “unstable,” with an aural need (i.e., musical tension) to resolve to a more stable musical consonance. Dissonance is quite variable between cultures and, even within Western music, between musical styles (e.g., jazz vs. rock). Although dissonance may be associated with “unpleasant” sounding chords and harmonies, it is able to add complexity, richness, and nuance to many melodies, especially when the dissonance is allowed to resolve toward consonance during the conclusion of the song.

Music is perceived in the same manner as any other sound in our environment and must be processed via the tympanic membrane, middle ear ossicles, cochlea, VIIIth cranial nerve, ascending auditory pathways, and primary auditory cortex (see Fig. 2.6) (Parent 1996; Ryland 2009). Music will produce a complex mixed

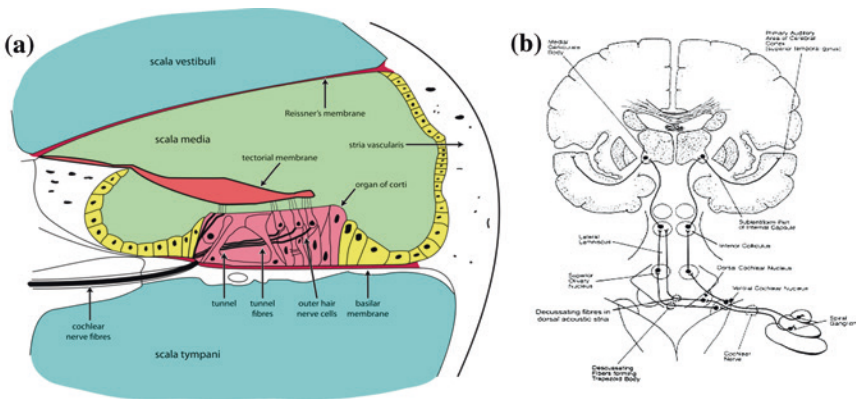


Fig. 2.6 **a** Cross section of the cochlea, demonstrating the organ of Corti and tectorial membrane within the scala media. Adapted from Wikipedia. **b** The auditory pathway begins in the cochlea and then travels via cranial nerve VIII (i.e., cochlear nerve) to the brainstem, where it passes through relay nuclei including the ventral and dorsal cochlear nuclei, superior olivary nuclei, inferior colliculi, and medial geniculate bodies, before terminating in the primary auditory cortex, which is located in the superior temporal gyrus. See text in Sect. 2.1 for further details

frequency sound wave that will interact with the tympanic membrane of both ears, thereby transmitting an acoustic signal to the ossicles of the middle ear. The ossicles of the middle ear consist of the malleus, incus, and stapes and are responsible for transferring the acoustic signal, through the oval window, into a hydraulic signal within the fluid of the inner ear and cochlea. Since the tympanic membrane has a surface area approximately $17\times$ greater than the oval window, the ossicles allow for the sound pressure of the acoustic signal to be concentrated, with a pressure gain of at least $20\times$ as it is transmitted to the cochlea. This gain is a form of impedance matching, since it takes more energy and pressure to move pressure waves through a liquid media than through air.

The cochlea consists of a fluid-filled coil tube of two and a half turns, and functions as an auditory transducer. Internally, the cochlea is partitioned into the scala vestibuli, scala tympani, and scala media (or cochlear duct) by the basilar and vestibular membranes. Sound energy is transmitted to the perilymph within the scala vestibuli through the round window via the foot plate of the stapes. The auditory transducing instrument is the *organ of Corti*, which lies within the scala media (surrounded by endolymph) on top of the basilar membrane, and consists of one row of inner hair cells and three rows of outer hair cells. The inner hair cells provide the main neural output of the cochlea, while the outer hair cells function as a preamplifier, receiving input from the brain that modifies the activity of the organ of Corti.

Overhanging the organ of Corti is the tectorial membrane, which is in contact with the hair cells. Sound energy transmitted to the perilymph through the oval window will set up traveling fluid waves within the scala vestibuli that correspond to the same frequencies as the acoustic signal. The fluid waves propagate from the base of the cochlea toward the apex, where the scala tympani and scala vestibuli merge (i.e., helicotrema). Because the vestibular membrane is so thin and delicate, the scala vestibuli and scala media function as a singular hydraulic unit as sound waves are propagated down the cochlea. The fluid waves within the endolymph of the scala media peak at a specific distance from the oval window, depending on their inherent frequencies, thereby causing vibrations and displacing the basilar membrane. Movement of the basilar membrane causes vibrations and movement of the overlying organ of Corti, with stimulation of the hair cells in that region of the cochlea. The organ of Corti functions as an audio frequency analyzer and is tonotopically organized, so that the highest frequency sounds maximally stimulate hair cells in the most basal portion of the cochlea, where the basilar membrane is narrow. Tones with the lowest frequencies maximally stimulate hair cells in the apical regions of the cochlea. Movement of the outer hair cells further amplifies the vibrations within the organ of Corti, resulting in stimulation of the inner hair cells. Once the inner hair cells have been stimulated, they depolarize via an influx of K^+ through channels near the tip region, resulting in activation of dendrites from bipolar afferent nerves located within the spiral ganglion (i.e., cochlear portion of the vestibulocochlear nerve; CN VIII). Most cells of the spiral ganglion innervate a section of the basilar membrane that is only a single hair cell in width, corresponding to the frequency it is designed to respond to.

The cochlear nerve, which consists of the central processes of the cells in the spiral ganglion, travels medially from the inner ear and enters the brainstem at the junction

of the medulla and pons (Parent 1996; Ryland 2009). As the nerve enters the brainstem, it bifurcates and makes synaptic connections with neurons in the dorsal and ventral cochlear nuclei. Both cochlear nuclei are tonotopically organized, but have different cellular components and cytoarchitecture. Neurons responding to higher frequencies are more dorsal, while those responding to lower frequencies are ventral.

There are three efferent projections from the cochlear nuclei: the dorsal, intermediate, and ventral acoustic striae. The dorsal acoustic stria originates from the dorsal cochlear nucleus and crosses over to the contralateral side, to join the fibers of the lateral lemniscus. The intermediate acoustic stria originates from the ventral cochlear nucleus and has a course similar to the dorsal stria, crossing over to join the lateral lemniscus. The ventral acoustic stria passes medially to terminate in the ipsilateral and contralateral nuclei of the trapezoid body and superior olivary nuclei, which then project fibers into the ipsilateral and contralateral lateral lemniscus. The fibers of the lateral lemniscus travel rostrally through the brainstem, mainly terminating in the nucleus of the inferior colliculus and the medial geniculate nucleus, along with a few fibers that terminate in the nearby nuclei of the lateral lemniscus. Some of the fibers of the lateral lemniscus bypass the inferior colliculus and project directly to the medial geniculate as the central acoustic tract. A tonotopic organizational structure is maintained within the nuclei of the inferior colliculus and medial geniculate body. Efferents from the nucleus of the inferior colliculus project rostrally through the brachium of the inferior colliculus to terminate in the medial geniculate nucleus.

The medial geniculate bodies are special sensory nuclei of the thalamus and are the final relay station of the hearing pathway. The efferent projections from the medial geniculate bodies form the auditory radiations (i.e., geniculocortical fibers), which travel to the ipsilateral temporal lobes, into the anterior transverse temporal gyri (i.e., gyrus of Heschl; Brodmann area 41), which is considered the location of the primary auditory cortex. The gyri of Heschl (HG) are located on the dorsal surface of the superior temporal convolutions and are partly buried in the lateral fissure. Cytoarchitectonically defined primary auditory cortex is located in the medial portion of HG, running anterolaterally in the plane. Lateral to the primary auditory cortex in HG are secondary auditory cortical regions. Behind HG lies the planum temporale (PT), which is considered to be an auditory association area. Basic processing of sound occurs at lower levels of the auditory pathway, so that the primary auditory cortex is not required for crude discrimination of sound frequency and intensity. However, it is necessary for processing the temporal patterns of sound and for determining sound direction, as well as for allowing higher level processing of complex sounds (e.g., music) in other functionally related brain regions (Metherate et al. 2005; Nelken 2008).

2.2.2 Neuroanatomy of Musical Processing and the Brains of Non-musicians

Early theories about the neurological aspects of musical processing, in the 1960s through 1980s, involved the concept of hemispheric specialization, and the idea that the left and right hemispheres had very distinct functions, some of which

were very compartmentalized, such as language in the left hemisphere and emotional responsivity in the right hemisphere (Walker 1980; Kyle 1988). Based on this framework, musical abilities and music processing were thought to be predominantly a right-hemispheric function for many years (Berman 1981). It was not until more detailed studies of patients with brain lesions (e.g., strokes, gunshot wounds), degenerative diseases (e.g., Alzheimer’s Disease, frontotemporal dementia), and congenital and acquired amusia, along with study of normal subjects using functional imaging techniques [i.e., functional MRI, magnetoencephalography (MEG), PET], that it became apparent that the neural analysis of music was more diffuse and bi-hemispheric (Peretz and Coltheart 2003; Peretz and Zatorre 2005; Griffiths 2001; Limb 2006). Many experts in the field, including Peretz, Griffiths, and Limb, are now suggesting that musical perception and analysis by the brain is a more modular process that can be broken down into smaller components, especially when using modern functional imaging techniques. This has led to the proposal of a cognitive model of musical processing by Peretz and colleagues (see Fig. 2.7), that is a preliminary attempt to demonstrate how musical acoustic inputs are analyzed and compartmentalized into distinct neuropsychological components (Peretz and Coltheart 2003; Stewart et al. 2006). The core of the model contains compartments for pitch analysis and temporal analysis, along with

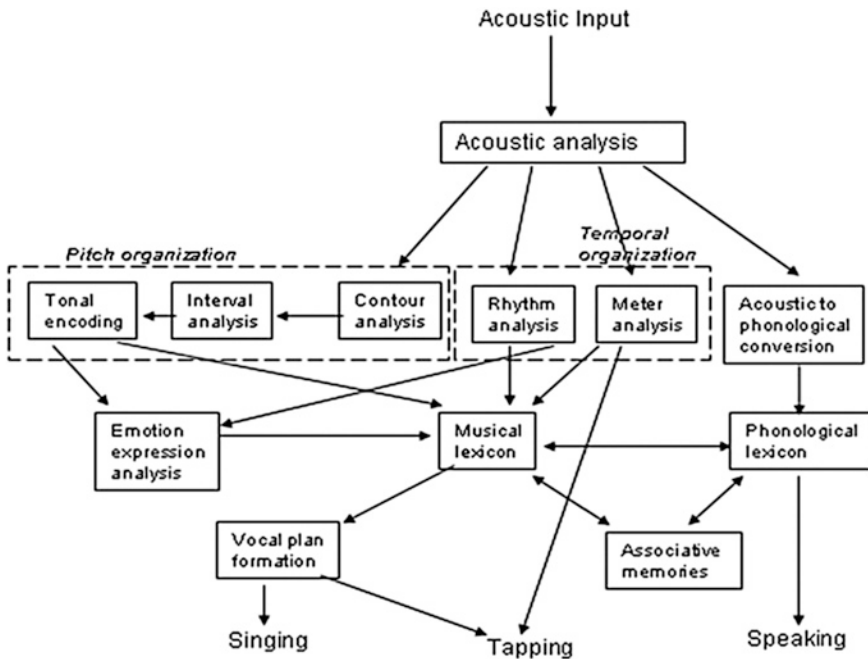


Fig. 2.7 Model of music processing as proposed by Peretz and colleagues. The musical acoustic signal is initially analyzed in parallel in the “pitch organization” and “temporal organization” compartments, followed by further processing for emotional expression, comparisons with the musical lexicon and phonological lexicon, and evaluations for associative memories. Adapted from Herdener et al. (2014), Hoppe (1988)

other aspects of musical processing. However, the model is somewhat simplistic and does not take into account many other aspects of the musical acoustic signal and music processing (e.g., timbre, harmony, beat) that have been studied in patients and normal subjects. In the following sections, we will review in detail the different structural components of music (as discussed in Sect. 2.1), and how these components are analyzed and processed within the primary and secondary auditory cortices, and related music-specific neural networks.

The most extensively studied aspects of musical structure have involved pitch perception, pitch contour, and melody (Griffiths 2001; Limb 2006; Stewart et al. 2006; Tramo et al. 2005). Although not all of the results have been consistent, the majority of studies varying pitch, pitch strength, and pitch structure have demonstrated activation in the secondary cortex in lateral HG, instead of primary auditory cortex (Gutschalk et al. 2002; Patterson et al. 2002; Penagos et al. 2004; Griffiths 2003). In addition, the report from Gutschalk et al. (2002) also noted that a region just posterior to the PT was very sensitive to the sound level and loudness of a given pitch stimulus, as opposed to its absolute pitch or regularity (Gutschalk et al. 2002). These studies and others have suggested the possibility of a “pitch center” in the lateral HG region, responsible for primary pitch processing of complex auditory inputs (Stewart et al. 2006; Griffiths 2003; Bendor and Wang 2006; Puschmann et al. 2010). For example, one recent study using fMRI techniques had subjects listen to pure tones in noise and dichotic pitch sequences and demonstrated pitch-related neural activation in the lateral end of HG in both hemispheres (Puschmann et al. 2010).

These findings and conclusions have been supported by neuronal recording studies in primates, which also suggest the existence of a “pitch center” within the secondary auditory cortex lateral to HG (Bendor and Wang 2005). Other work in primates, cats, and similar animals suggest that frequency-sensitive neurons in the primary auditory cortex may also contribute to basic pitch perception; for example, the ability to aid in fine-grained pitch discrimination or detect the direction of pitch change (i.e., higher or lower) (Tramo et al. 2005). A more recent study in non-musicians using fMRI techniques and multivariate pattern analysis examined pitch contour discrimination using variable ascending and descending melodic sequences (Lee et al. 2011). They also identified the right superior temporal sulcus region as being highly activated in this setting. In addition, there was also significant activation within the left inferior parietal lobule and the anterior cingulate cortex. Although the data presented above seem fairly consistent, a new report by Barker and colleagues using fMRI techniques challenge the concept of a “pitch center” in the lateral HG and state it might be artifactual, based on previous studies using the wrong kind of auditory stimuli, which contain slowly varying spectrotemporal modulations unrelated to pitch (Barker et al. 2012). Further research into the functional anatomy and neurobiology of primary pitch processing will be necessary before any final conclusions can be drawn.

When the brain is processing musical auditory inputs that involve more complex pitch structures such as melodies, chords, and harmonies, the analysis must be able to dissect the global structure of the auditory signal (i.e., pitch contour; the pattern of “ups and downs”), as well as the more local level of the precise pitch intervals that comprise the contour (Griffiths 2001; Limb 2006; Stewart et al. 2006; Tramo et al. 2005). Early evidence from neuroanatomically based lesion studies in patients (e.g., post-stroke,

frontotemporal degeneration, epilepsy surgery) suggested that processing of the global structure and pitch contour would occur in the right posterior superior temporal cortex, in advance of local processing within the left posterior superior temporal cortex (Peretz 1990; Liégeois-Chauvel et al. 1998). These analyses would be hierarchically linked, such that the pitch contour would have to be analyzed first, to provide an acoustic context for the signal, followed by processing of the local structure and fine detail to place within the global framework.

In a study to evaluate this process in normal healthy subjects, Stewart and co-workers used fMRI, while participants listened to consecutive pitch sequences and performed a same/different one-back comparison task (Stewart et al. 2008). When sequences were different, they either preserved (locally different) or violated (globally different) the contour of the sequence preceding them. The results showed that during global pitch contour processing, there was activation of the left PT and posterior superior temporal sulcus (pSTS) region. In contrast, during local pitch processing, there was bilateral activation of the PT and pSTS regions (see Fig. 2.8). Therefore, the brain seems to be able to analyze pitch contour and the

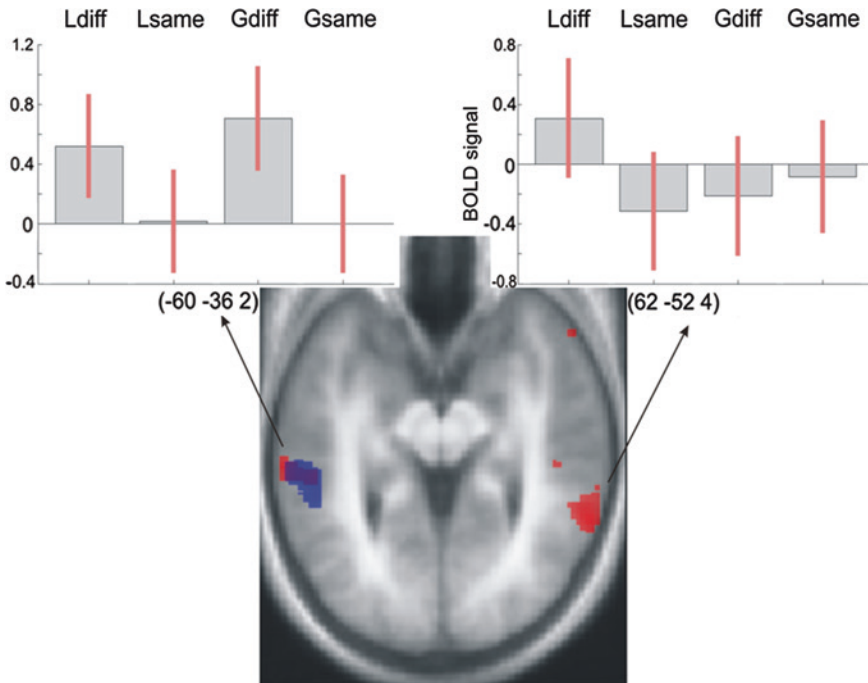


Fig. 2.8 fMRI results in a non-musician subject during global pitch contour processing and local pitch interval processing. During the global pitch contour processing, there was activation of the left PT and posterior superior temporal sulcus (pSTS) region (seen in blue). In contrast, during local pitch interval processing, there was bilateral activation of the PT and pSTS regions (seen in red). See text in Sect. 2.2 for further details. Adapted from Kunej and Turk (2000), with permission from the senior author

global structure of a pitch sequence while only using the left PT and pSTS, while for local pitch processing, more neural resources are required so that the bilateral PT and pSTS regions require activation. Although these results are not entirely consistent with the older, anatomically based studies in neurologically impaired patients, they are still supportive of the hierarchical model that proposes initial global processing of pitch contour, followed by processing of more detailed local pitch structure, within the PT and pSTS regions of the brain. It is likely that the neural pitch processing apparatus noted above is not specific to music, but is also critical for analysis of the pitch changes necessary for language and the linguistic interpretation of prosody.

Numerous other studies have been performed to evaluate different aspects of musical auditory signal processing, such as pitch, melody, timbre, and time structure (Griffiths 2001; Limb 2006; Stewart et al. 2006; Tramo et al. 2005). Several studies have used fMRI techniques to analyze neural processing of basic pitch and melody, using different auditory stimuli (Gutschalk et al. 2002; Puschmann et al. 2010). In one report, pure tones in noise or dichotic pitch sequences, which either contained a fixed pitch or a melody, were used in normal subjects (Puschmann et al. 2010). They noted activation of the lateral end of HG in both hemispheres during processing of dichotic pitch sequences. When the dichotic pitch stimuli contained a melody, the activation was more evident in the PT and the planum polare (anterior portion of the superior surface of the superior temporal gyrus), but not in primary auditory cortical regions. In a similar study, the auditory stimuli were spectrally matched sounds that produced no pitch, fixed pitch, or a melody (Patterson et al. 2002).

All of the different auditory stimuli were noted to activate HG and PT, although sounds with pitch produced more activation in the lateral half of HG in comparison with sounds without pitch. When the stimulus contained a melody, neural activation beyond HG and PT was noted, more laterally within the superior temporal gyrus and planum polare. The authors concluded that there was a hierarchy of pitch processing in the brain, such that as the auditory stimuli become more complex (e.g., basic pitch sequences vs. melody), the center of activation moves anteriorly and laterally away from primary auditory cortex. Another fMRI study scanned volunteers as they were listening to pure-tone melodic-like sequences, while the pitch distances between consecutive tones were varied in a parametric fashion (Hyde et al. 2008). They noted that the right PT was linearly responsive to increasing pitch distance, even when the change in pitch was very subtle. In contrast, the degree of activation in the left PT was relatively constant as a function of pitch distance, except at the largest pitch change. This study supports the model of the right secondary auditory cortex being more important for the processing of fine pitch resolution. In a study using PET techniques, designed to evaluate the ability of subjects to remember and compare melodic pitch sequences at different points, processing of pure melodies (versus noise bursts) resulted in activation in the right superior temporal and right occipital cortices (Zatorre et al. 1994). When subjects were required to remember and compare the first two notes of a pair of melodic pitch sequences, there was activation within the right inferior frontal opercular

region. In the most demanding task, subjects had to compare the pitch of the first and last notes of a pair of melodic sequences. In this task, there was further activation of brain regions, including the right frontal and right temporal lobes, as well as within the parietal and insular cortical regions.

In Western styles of music, the listener usually has a certain degree of expectation about the musical notes that will fit properly within a specific musical reference, in relation to the musical key, melody, harmony, and chord structure (Peretz and Zatorre 2005; Griffiths 2001; Limb 2006). This kind of expectant relational pitch framework can be considered “musical syntax” and is analogous to the syntactical rules necessary for analysis of language. Violations of these musical expectancies are considered violations of musical syntax, in which the listener is able to pick out a note or chord that does not fit within the given key (e.g., melody in C major, but C# is used instead of C natural).

Several studies have now suggested that neural processing of musical syntax occurs in the frontal lobes, within or near Broca’s area, which is critical for the syntactic processing of language (Maess et al. 2001; Janata et al. 2002; Koelsch and Siebel 2005). In a study using MEG, Maess et al. (2001) presented a series of chords to non-musician listeners, some of which had out-of-key notes but still maintained the proper major or minor chord structure (i.e., Neapolitan chords). The Neapolitan chords resulted in the presence of an early effect called the magnetic equivalent of the early anterior negativity (mERAN), since it was analogous to EEG studies which show an ERAN in response to musical syntactic violations. The source of the mERAN was localized to Broca’s area and its right hemisphere homolog. Other studies using fMRI suggest that more mesiofrontal regions are important for monitoring the key of a given piece of music, as well as the history of keys being processed in the melody (Janata et al. 2002; Koelsch and Siebel 2005). Overall, these kinds of studies support the notion of musical syntax and imply that the neural processing of musical syntax involves Broca’s area and nearby regions of the frontal lobes, which have traditionally been thought to only be important for language.

As mentioned above, timbre is the quality of a sound that allows the listener to discriminate between different sound sources and different musical instruments (Surmani et al. 2004). Differences in spectral envelope, harmonics, attack, and other sound qualities account for the timbre of various instruments. An early study using PET evaluated the structural components of musical perception, including timbre, during a series of musical tasks (Platel et al. 1997). For the timbre task, two synthesized timbres in the sound spectrum of an oboe were used and presented in various patterns. During the timbre tasks, there was predominant activation of the right hemisphere, mainly within the superior frontal gyrus and middle frontal gyrus. In contrast, more recent studies using fMRI suggest that the temporal lobes are the primary brain regions involved in the neural processing of timbre (Warren et al. 2005; Menon et al. 2002; Samson 2003; Halpern et al. 2004). In a general study of the neural processing of the spectral envelope of different sounds, changing either the pitch or the spectral envelope of harmonic sounds activated the HG and adjacent regions of the superior temporal lobes bilaterally (Warren et al. 2005).

Changing the spectral envelope of continuously alternating noise and harmonic sounds resulted in additional right-lateralized activation in the superior temporal sulcus. Using musical sound stimuli in which several aspects of timbre were altered simultaneously, Menon and co-workers noted significant activation in posterior HG and superior temporal sulcus, with some extension into the circular insular sulcus (Menon et al. 2002). No significant difference was present between right and left hemispheric activation. However, there was a more posterior predilection for activation in the left temporal lobe in comparison with the right temporal lobe, suggesting a functional asymmetry. In a study of perceived versus imagined timbre, subjects had to make comparative judgments of timbral characteristics of musical instrument sounds (Halpern et al. 2004). During the perceptual timbre tasks, there was activation of primary and secondary auditory cortices, with a mild right-sided asymmetry. During the timbre imagery task, activation of secondary auditory cortical regions was noted, with significant overlap with the perceptual task findings. Overall, the available studies would suggest that brain processing of musical timbre is performed within a neural network that extends along the superior temporal gyrus, including both anterior and posterior regions, with a possible mild right-sided predominance (Samson 2003). The frontal lobes may also play a minor role in neural processing of musical timbre.

The neural processing of the temporal organization of music (i.e., rhythm, meter, beat, tempo) has not been as clearly delineated as the processing of pitch perception Herholz and Zatorre (2012); Herholz et al. (2012); Hetland (2000). Earlier studies investigated the temporal aspects of music by having subjects respond to and reproduce progressively complex rhythms (Penhune et al. 1998; Griffiths et al. 1998; Sakai et al. 1999). In a PET study, activation was noted in the lateral cerebellar cortex and cerebellar vermis during the performance of timed motor responses, especially when the stimulus to be reproduced was complex (Penhune et al. 1998). The basal ganglia structures were also activated during the task, but to a lesser degree. In a fMRI study, Griffiths and colleagues used a “delay-and-add” noise strategy, which is supposed to activate all frequencies uniformly, similar to noise, but can also produce strong pitch perceptions and melodies (Griffiths et al. 1998). The sound stimulus also had temporal regularity which could be systematically altered. They noted that the primary auditory cortex was activated in proportion to the regularity of the stimulus. When the sound stimulus contained a melody as well as temporal regularity, activation was also present in areas outside of the primary auditory cortex region (i.e., more posteriorly into secondary auditory cortex).

Another fMRI-based study attempted to compare auditory stimuli that varied based on metrical and non-metrical representations of rhythms formed with small integer and non-integer ratios (Sakai et al. 1999). During the integer-based auditory tasks, which is more representative of music, there was increased activity present in the anterior lobe of the cerebellum. Several recent studies using fMRI corroborate the involvement of the cerebellum and related pathways in the neural processing of temporal structure and auditory timing (Xu et al. 2006; Teki et al. 2011). During the perception and motor performance of temporal sequences, fMRI

was used to dissociate the perceptual from the motor aspects of timing (Xu et al. 2006). The results demonstrated the activation of multiple areas within the cerebellar cortex during the perception tasks and the motor performance tasks. In addition, it was noted that the inferior olive was activated only when the subjects perceived the temporal sequences, without any associated motor activity. This suggests a primary role for the olivo-cerebellar climbing fiber system in the encoding of temporal information, independent of motor behavior. In a similar study, subjects were asked to judge the difference in duration of two successive time intervals as a function of the preceding context of an irregular series of clicks or a regular series of clicks (Teki et al. 2011). During the absolute, duration-based timing tasks, there was activation of the olivo-cerebellar network, including the inferior olive, vermis, and deep cerebellar nuclei (i.e., dentate nucleus). In contrast, during the relative, beat-based timing tasks, there was activation of a striato-thalamo-cortical network, including the putamen, caudate nucleus, thalamus, supplementary motor area, premotor cortex, and dorsolateral prefrontal cortex. Therefore, these results suggest two distinct neural timing mechanisms and sub-systems: one involving the olivo-cerebellar pathways that acts as a precision clock to mediate duration-based timing, and another that involves a striato-thalamo-cortical network that mediates relative, beat-based timing. A recent fMRI study had subjects find and tap to the beat of rhythms that were varied from metrically simple to metrically complex (i.e., from a strong to a weak beat) (Kung et al. 2013). The beat finding and beat tapping activity activated overlapping brain regions that included the superior temporal gyrus, premotor cortex, and ventrolateral prefrontal cortex (VLPFC). Beat tapping activity in the superior temporal gyrus and VLPFC was correlated with both perception and performance, suggesting that they were important for retrieving, selecting, and maintaining the musical beat.

Basal ganglia activation was noted as well, but was similar in all conditions and did not correlate with either perception or production of the beat. Not all of the studies have been consistent, since another report using fMRI to monitor subjects responding to music that was either intact or scrambled suggested activation in the temporal lobes (Fedorenko et al. 2012). All subjects listened to passages of intact music, scrambled music, pitch scrambled music, and rhythm scrambled music, as well as linguistic tasks. Intact music induced more potent activation in the brain than scrambled music, involving the anterior STG bilaterally, posterior superior and middle temporal gyri bilaterally, premotor regions, and the supplementary motor areas. When the pitch structure was scrambled or the rhythmic structure was scrambled, similar but less significant activation was noted bilaterally in the temporal lobes. Linguistic tasks did not activate these regions of the brain. Similarly, a study by Limb et al. (2006) used fMRI to study passive rhythm perception in non-musicians and musicians. Subjects were required to listen to regular and random rhythmic patterns, without any verbal or motoric responses. A pattern of activation was noted in a network responsible for rhythm perception in the bilateral superior temporal regions, left inferior parietal lobule, and the right frontal operculum, in both non-musicians and musicians. Some laterality was noted in the musicians, which will be described in the next section.

Since music is so ubiquitous in most modern societies, the average teenager or adult will have a vast repertoire of songs and musical passages that are familiar and can be easily recognized or imagined in their mind. The neural representations of these songs, melodies, and musical phrases are stored in a music-specific memory system that has been termed the “musical lexicon” by Peretz and colleagues (2003, 2005, 2006). Neuroscientists have attempted to localize the neural structures responsible for recognizing songs and melodies for many years, initially in patients with brain damage (Peretz 2006; Peretz and Zatorre 2005; Griffiths 2001). The brain damage literature (e.g., stroke, Alzheimer’s, frontotemporal degeneration) suggests that deficits in the perception and recognition of familiar songs and melodies can arise with injuries involving the right or left anterior STG and insula, while the more specific loss of the ability to recognize familiar tunes seems to involve damage to the right insula (Griffiths 2001; Ayotte et al. 2000).

Early studies of intact subjects using PET techniques, scanned while each was engaged in a task of imagining the continuation of a tune after hearing a short series of notes (Halpern and Zatorre 1999). There was activation primarily on the right side in the frontal and superior temporal regions, plus the supplementary motor area. During the retrieval of real tunes, there was activation mainly in the right frontal areas and right superior temporal gyrus. Similar results have been described in a series of fMRI studies using intact subjects (Rauschecker 2005; Janata 2005; Peretz et al. 2009; Schulze et al. 2011; Herholz et al. 2012). In one study, subjects were asked to anticipate the continuation of music from very familiar songs and imagine the appropriate sequence of notes versus actually hearing the complete musical passage (Rauschecker 2005). Activation was noted in the right anterior superior temporal cortex, right inferior frontal cortex and anterior insula, left anterior prefrontal cortex, lateral cerebellum, and the anterior cingulate. In a similar study, Herholz et al. (2012) asked subjects to view the lyrics of familiar tunes, while listening to the song or imaging the music, during fMRI evaluation.

There was significant overlap during melody perception and imagery, including activation of the secondary auditory cortices. During the imagery task, an extended network was activated, including prefrontal cortex, supplementary motor areas, intra-parietal sulcus, and the cerebellum. In addition, during the musical imagery task, there was increased functional connectivity of the anterior right temporal cortex with the frontal areas, suggesting these regions form an imagery-related network. Using a different experimental paradigm with fMRI, Peretz and colleagues studied non-musician subjects, while they listened to familiar musical themes, unfamiliar music, or random tones. All of the stimuli were synthesized and played with the sound of a piano. While listening to familiar musical passages, there was focal activation in the right superior temporal sulcus region. In addition, these auditory memories were tightly coupled with action (e.g., singing), by demonstrating left-sided activation of the PT, supplementary motor areas, and inferior frontal gyrus. In a study by Schulze and co-workers, fMRI was used to examine verbal and tonal working memory (WM) in a cohort of non-musicians and musicians (Schulze et al. 2011). It was theorized that non-musicians would be trained

in speech and verbal domains, but not in music, while musicians would be trained in both domains. It was noted that core structures of WM were involved in both tonal and verbal WM in non-musicians and musicians, including Broca's area, premotor cortex, presupplementary motor area and supplementary motor area, left insular cortex, and inferior parietal lobe. In musicians, additional activation was noted in the right insular cortex during verbal WM tasks, as well as in the right globus pallidus, right caudate nucleus, and left cerebellum during tonal WM tasks. These results suggest two different WM systems in musicians: one for verbal and phonological information and another for melodic and tonal information.

The ability of music to evoke and inspire specific emotions is well recognized, and one of the most powerful reasons that music remains so pervasive in cultures throughout the world and for so many individuals (Peretz and Zatorre 2005; Griffiths 2001; Limb 2006). As mentioned above in Sect. 2.2, many investigators now think that music, and in particular song-like vocalization, was a proto-language that predated modern speech and language during the evolution of *Homo sapiens* (Peretz 2006; Masataka 2009). As part of that process, some vocalizations became less emotional and more semantic, evolving into language, while the other pathway preserved the emotional connections along with semantic ambiguity and evolved into music (Perlovsky 2010). Lesion-based studies investigating the loss of enjoyment or lack of emotional response to music in patients with various disease processes (e.g., stroke, Alzheimer's disease, neurodegenerative diseases, surgical resection) have most consistently noted damage involving the left or right medial temporal lobe, amygdala, and insula (Griffiths 2001; Omar et al. 2011). For example, in a recent study of patients with frontotemporal dementia, lack of emotional responses to music was correlated with a loss of gray matter in a network that included the insula, orbitofrontal cortex, anterior and posterior temporal cortices, amygdala, and subcortical mesolimbic connections (Omar et al. 2011).

It is now becoming apparent from functional studies (i.e., PET, fMRI) in normal subjects that the neural basis of music-evoked emotions involves connectivity between the networks that mediate musical perception and more primitive mesolimbic structures (Griffiths 2001; Blood et al. 1999; Blood and Zatorre 2001; Brown et al. 2004; Menon and Levitin 2005; Koelsch 2010; Salimpoor et al. 2011). Early studies by Blood and colleagues used PET scans and measurements of alterations in cerebral blood flow that were related to affective responses to music (Blood et al. 1999; Blood and Zatorre 2001). In the first study, they had subjects listen to six versions of a novel musical passage while varying the degree of melodic consonance and dissonance (Blood et al. 1999). Blood flow alterations were noted in the right parahippocampal gyrus, right precuneus, bilateral orbitofrontal regions, medial subcallosal cingulate, and the right frontal polar regions. The amount of blood flow alteration correlated with the degree of perceived pleasantness or unpleasantness of the musical passages. Another study used PET to evaluate subjects while listening to intensely pleasurable music that could cause "chills" or send "shivers down the spine" (Blood and Zatorre 2001). As the intensity of the chills increased, blood flow alterations were noted in ventral striatum, midbrain, amygdala, orbitofrontal cortex, and ventral medial prefrontal cortex.

All of these brain regions are known to be involved in the neural circuitry mediating reward, motivation, emotion, and arousal and are also known to be active in response to other euphoria-inducing stimuli, including food, sexual activity, and drugs of abuse (Koelsch 2010).

Using a different study paradigm, Brown et al. (2004) used PET to evaluate subjects while listening to unfamiliar but strongly pleasurable instrumental music (Brown et al. 2004). They noted activation in the subcallosal cingulate gyrus, prefrontal anterior cingulate, retrosplenial cortex, hippocampus, anterior insula, and nucleus accumbens. Activation was also noted in the primary and secondary auditory cortices, and temporal polar regions. This was the first study to demonstrate that spontaneous, passive listening to pleasurable music could activate limbic and paralimbic structures and circuitry. In a combined PET and fMRI study, Salimpoor and co-workers analyzed subjects while listening to music well known to cause “peak listening” experiences (Salimpoor et al. 2011). Using [(11)C] raclopride PET, it was shown that dopamine was released into the striatum at the peak of emotional arousal in response to the music. fMRI was then used to plot the time course of dopamine release and showed a functional dissociation: during the anticipation phase, leading up to the peak musical phrases, dopamine release was mainly in the caudate nucleus, while during the peak emotional phase, the nucleus accumbens was more involved. Using fMRI and connectivity analysis in subjects while listening to pleasurable music, Menon and Levitin noted strong activation of the nucleus accumbens, ventral tegmental area, hypothalamus, and insula (Menon and Levitin 2005). Activation was strongly correlated between the nucleus accumbens and ventral tegmentum, as well as between the nucleus accumbens and hypothalamus. Functional connectivity analysis suggested significant ventral tegmentum-mediated interaction of the nucleus accumbens with the insula, hypothalamus, and orbitofrontal cortex. In addition, several investigators have examined the role of emotional arousal in the musical listening experience and have found that the degree of emotional arousal correlates strongly with ratings of pleasure, as well as with how memorable a given piece of music is over time (Salimpoor et al. 2009; Eschrich et al. 2008).

2.2.3 Neuroanatomy of Musical Processing and the Brains of Musicians

For centuries anatomists, physicians, and neuroscientists have investigated potential differences between the brains of musicians and non-musicians, assuming there must be some quantifiable parameters that correlate with musical expertise and skill (Griffiths 2001; Stewart et al. 2006; Dawson 2011; Bentivoglio 2003; Schlaug 2003). The earliest reports focused on anatomical studies of famous musicians from the nineteenth and early twentieth centuries (e.g., Hans von Bulow, Bernhard Cossmann) (Bentivoglio 2003; Meyer 1977; Auerbach 1906–1913). Some of the anatomical studies concluded that there were differences in the

middle and posterior thirds of the superior temporal gyrus, as well as in the supramarginal gyrus, in the brains of these famous musicians. In the modern era, using advanced imaging techniques such as PET, fMRI, volumetric MRI, MRI tractography, functional connectivity analysis, and MEG, the anatomical and functional differences between musicians and non-musicians are becoming more clearly elucidated. Several regions of the brain have been shown to be different in musicians, including the cerebellum, corpus callosum, auditory cortices, motor regions, somatosensory cortex, and superior parietal region (Dawson 2011; Schlaug 2003).

Hutchinson et al. (2003) studied the brains of a group of professional keyboard players and compared them to matched non-musician controls, using volumetric MR imaging (Hutchinson et al. 2003). There was significantly greater absolute and relative cerebellar volume (10.4 % vs. 9.9 %), but not total brain volume, in the male musicians. Relative cerebellar volume was also correlated with the degree of lifelong intensity of practice in the male musicians. In the female group, there was no significant difference in cerebellar volume noted between musicians and non-musicians. Several research groups have documented differences in the size of the corpus callosum between musicians and non-musicians, including an age-related effect (Schlaug et al. 1995; Lee et al. 2003; Ozturk et al. 2002; Steele et al. 2013). Schlaug and colleagues were the first to report this difference, when they studied 30 musicians and compared them to age-, sex-, and handedness-matched controls using in vivo MR morphometry (Schlaug et al. 1995). The anterior half of the mid-sagittal corpus callosum was significantly larger in musicians than non-musicians (mean 371 mm² vs. 344 mm²). This effect was most prominent in the subgroup of musicians who had begun their musical training before the age of 7 (≤ 7 years = 384 mm²). A follow-up study from the same group, with an enlarged cohort of musicians ($N = 56$), noted similar findings (Lee et al. 2003). However, in the larger study, the enlargement of the anterior mid-sagittal corpus callosum was most significant in the male musicians, but not in female musicians. The lack of enlargement in the female musicians was felt to be related to a tendency for a more symmetric brain organization in females, as well as a disproportionately high representation of absolute pitch musicians among females. In a similar MRI study of 20 musicians and matched controls, a Turkish group noted significant increases in volume of the anterior and posterior portions of the corpus callosum in the musician cohort (Ozturk et al. 2002). Overall thickness of several regions of the corpus callosum was also greater in the musician group than in controls.

A recent study evaluated the onset of musical training in terms of the white matter organization of the corpus callosum in musicians (Steele et al. 2013). Using diffusion tensor imaging MRI, early- and late-trained musicians matched for years of training and experience were analyzed. In the early-trained group, there was greater connectivity in the posterior midbody/isthmus of the corpus callosum. Fractional anisotropy in this region was related to the age of onset of training and sensorimotor synchronization performance. The authors concluded that onset of musical training before age 7 was associated with changes in white matter connectivity in the brain. The primary and secondary auditory cortices also appear to be anatomically and functionally different in musicians (Dawson 2011; Schlaug

2003). Using MEG techniques Schneider et al. (2002) compared the processing of sinusoidal tones in the auditory cortex of amateur and professional musicians and non-musicians (Schneider et al. 2002). In professional musicians as compared to non-musicians, the activity evoked in primary auditory cortex after stimulus onset was 102 % larger, and the gray matter volume of the anteromedial portion of HG was 130 % larger. Both of these quantitative changes were highly correlated with musical aptitude, as measured by psychometric evaluation. In a different experimental paradigm using scrambled pieces of piano music, musicians and non-musicians appeared to process the auditory signals differently (Matsui et al. 2013). Non-musicians had activation of only the right STG, while musicians had activation of the right and left STG. It was suggested that left STG activation was induced in musicians because the auditory stimuli were musically related. In a study of musicians and non-musicians using fMRI during a passive musical listening task, Ohnishi and co-workers also noted a functional difference in auditory processing (Ohnishi et al. 2001). In musicians, there was predominant activation of the left secondary auditory cortex and the left posterior dorsolateral prefrontal cortex. In contrast, non-musicians had activation of the right secondary auditory cortex for the same task. In addition, there was activation of the bilateral PT in the musician cohort. The degree of activation of the left PT correlated strongly with the age of onset of musical training (i.e., more activation with younger onset). Activation of the left PT was most pronounced in musicians with perfect pitch. In general, the PT is found to be larger (i.e., mean volume) in musicians in comparison with non-musicians (Schlaug 2003).

However, this does not appear to be true of all musicians, but only in the subgroup that have perfect pitch (Ross et al. 2005; Schlaug 2003; Zatorre 2003). Musicians with perfect pitch have a left-sided asymmetry and enlargement of the PT. The critical issues underlying the presence of perfect pitch remain unclear, but in most cases, it applies to musicians that started their musical training or were exposed to music before 7 years of age. The motor cortex has also been noted to have differences between musicians and non-musicians (Dawson 2011; Schlaug 2003). In musicians, there was enlargement of the right and left motor cortices, as measured by the sulcal length of the posterior bank of the precentral gyrus. The degree of enlargement was more pronounced in musicians that had begun musical training at a young age (i.e., before age 10) (Amunts et al. 1997). A similar study in right-handed violin players noted significant enlargement of the left motor and somatosensory cortices, in comparison with matched controls (Schwenkreis et al. 2007). Asymmetry of the motor and somatosensory cortices was highly correlated among the violin players. However, when performing non-musical tasks to test fine motor skills, the violinists performed similarly to the non-musician cohort. Using voxel-by-voxel MRI morphometry techniques, Gaser and Schlaug studied the brains of professional keyboard players, amateur musicians, and non-musicians (Gaser and Schlaug 2003). Gray matter volume was noted to be larger in the professional musician cohort, within the somatosensory cortex and the superior parietal cortex. There was also a strong correlation between gray matter volume in these regions and musician status, as well as the degree of practice intensity.

Some possibly reflecting its greater musicality these findings have been confirmed in a more recent study of professional pianists in China (Han et al. 2009). The pianist cohort had higher gray matter density in the left primary sensorimotor cortex and right cerebellum, in comparison with a matched non-musician group. In addition, the pianists also had higher fractional anisotropy (i.e., indicating higher white matter integrity) in the right posterior limb of the internal capsule.

Several groups have focused on white matter tracts and the plasticity of the brain in the context of musical training (Dawson 2011; Herholz and Zatorre 2012). It is now becoming clearer that musical training does induce brain plasticity within white matter structures, on a short-term and long-term basis. For example, the corticospinal tract has been studied by several investigators using diffusion tensor MRI. Bengtsson et al. (2005) studied 8 professional concert pianists and matched controls, and grouped them according to estimates on how much they had practiced during childhood, adolescence, and adulthood. Childhood practicing correlated with functional anisotropy (FA) in the bilateral limbs of the internal capsule, which include the corticospinal tracts, as well as the corpus callosum. The right posterior internal capsule was the only region with significantly higher FA values in the musician group compared to the non-musician group. Practice during adolescence correlated with FA in the splenium and body of the corpus callosum, while adult practice correlated with FA in the left anterior limb of the internal capsule, and possibly the right arcuate fasciculus. A similar report using diffusion tensor imaging techniques and fiber tractography studied professional musicians and controls, and found significantly lower FA values in the left and right corticospinal tract of the musician group (Imfeld et al. 2009). A right-greater-than-left asymmetry of FA was also noted, in both the musician and non-musician groups.

Among the musicians, diffusivity was negatively correlated with the onset of musical training in childhood, so that training with onset before age 7 was associated with increased diffusivity in comparison with the late onset subgroup and controls. Halwani et al. (2011) used similar techniques to study large white matter tracts, including the arcuate fasciculus, in professional singers, instrumentalists, and non-musicians (Halwani et al. 2011). Both singers and instrumentalists were found to have larger tract volume and higher FA in the right and left arcuate fasciculus in comparison with non-musicians. In comparison with the instrumentalists, singers had larger tract volume, but lower FA, in the left dorsal arcuate fasciculus, along with a similar trend for the left ventral arcuate fasciculus. In singers, the FA of the left dorsal branch of the arcuate fasciculus was inversely correlated with the number of years of vocal training. The same group has also studied the effects of instrumental musical training in young children over a 15 month period, using deformation-based MRI morphometry techniques (Hyde et al. 2009). In comparison with non-training controls, the training group developed increased volume within the motor cortex (i.e., hand area), corpus callosum, and the primary auditory areas over the 15-month testing period. The changes on the MRI scans were also correlated with improvements in musically relevant fine motor and auditory skills. Finally, there have been several studies evaluating how the brain analyzes rhythmical structure in musicians (Limb et al. 2006; Hyde et al. 2009). In the first report, an fMRI

evaluation of passive rhythm perception between musicians and non-musicians, it was noted that a different neural network was engaged in the musician group (Limb et al. 2006). There was a left-sided lateralization of activation involving the perisylvian cortices, in particular the frontal operculum, superior temporal gyrus, and inferior parietal lobule. The authors suggested that musical training leads to the employment of left-sided perisylvian brain areas that are typically active during language comprehension, during passive rhythm perception activities.

A similar fMRI study evaluated the neural processing of rule-based rhythmic structure in jazz drummers and non-musicians (Herdener et al. 2014). For all subjects, deviations from the regular rhythmic structure activated the left PT, along with Broca's area and its right-hemispheric homolog. This is part of the same network that is critically involved in the processing of harmonic structure in music and the syntactic analysis of language. However, only in the jazz drummer cohort, there was additional activation of the left supramarginal gyrus, a higher-order region usually involved in the processing of linguistic syntax. These findings suggest that the processing of complicated rhythmical patterns requires the functional recruitment of brain areas usually dedicated to the processing of complex linguistic syntax.

2.2.4 The Neurology of Musical Performance

Performing music in general, and in particular at the professional level, is one of the most difficult and complex of human endeavors (Altenmüller 2008, 2010; Parsons 2001; Wiesendanger 2010). Musical performance requires the integration of multimodality motor and sensory information, along with precise monitoring of the motor performance by ongoing auditory feedback. The musician is required to reproduce highly controlled movements with extreme precision and reliability and is constantly assembling, storing, and improving complex sensorimotor programs. These specialized sensorimotor skills require extensive training over many years, often starting at a young age. For musical skills to be developed at such a high level, the student not only has to have the necessary innate neuromuscular skill-set to play an instrument, but also has to have a nurturing and supportive home environment, be exposed to and form relationships with engaging and talented music teachers, and have early experiences with music that promote intense and positive emotional experiences (Sloboda 1993). To acquire the skills necessary to perform music at a professional level (e.g., rock guitarist, classical violinist, jazz pianist, drummer, bassist), it is estimated that the minimal threshold amount of practice is approximately 10,000 h.

During the years of practice required to attain this level of skill, numerous brain regions become robust and many neural connections are established (i.e., musically induced brain plasticity) between the involved areas. As noted above, it is now well established that music practice can enhance myelination, gray matter growth, and fiber connections of brain structures involved in specific musical activities (Dawson 2011; Schlaug 2003; Herholz et al. 2012). The integration

between sensorimotor and auditory cortical regions that develops after many years of practice is very strong. This has been demonstrated in an fMRI study of professional pianists, who were asked to listen to simple piano tunes without moving their fingers or other parts of their body, and to press the keys and play on a mute piano (Bangert et al. 2006). In comparison with the matched non-musician controls, while passively listening to the piano tunes, the pianists had activation of the appropriate motor (i.e., hand) and sensory regions as if they were actually playing the piano tunes themselves (i.e., motor co-representation). In addition, during the task of playing the mute piano, there was activation of an auditory association area between the temporal and parietal lobes that appears to function as an auditory–motor interface, translating the fingerings into the appropriate sounds.

A distributed cortical network was involved in both tasks, including the dorso-lateral and inferior frontal cortex (including Broca’s area), superior temporal gyrus (including Wernicke’s area), supramarginal gyrus, supplementary motor areas, and supplementary premotor areas. This type of music practice-induced sensorimotor–auditory co-activation can even be followed in non-musicians completely naïve to instrumental music (Bangert and Altenmüller 2003). Non-musicians who had never played an instrument before were trained on a computer piano twice a week over a 5-week period. Mild auditory–sensorimotor EEG co-activity was noted even after the first practice session and was significantly enhanced over the 5-week training cycle. By the end of the training, similar to the professional pianists, the cohort would have increased activity in the central and left sensorimotor regions when passively listening to piano tunes and would also have increased activity in the auditory regions of both temporal lobes while playing a mute piano. Parsons and colleagues have performed a PET study to evaluate the neural activation patterns of professional piano players while performing a memorized Bach concerto versus a series of memorized major scales (Parsons et al. 2005). During both performances, there was activation of primary motor cortex, corresponding somatosensory areas, inferior parietal cortex, supplementary motor areas, motor cingulate, bilateral superior and middle temporal cortex, right thalamus, and the anterior and posterior cerebellum. Regions that were activated more specifically for the concerto included the superior and middle temporal cortex, planum polare, thalamus, basal ganglia, posterior cerebellum, dorsolateral premotor cortex, right insula, right supplementary motor area, lingual gyrus, and posterior cingulate. There were also some areas of deactivation noted for each performance, which were more prominent for the concerto, possibly reflecting its greater musical complexity and difficulty.

2.2.5 Jazz Musicians and the Neurology of Musical Improvisation

Jazz is a very popular and unique form of music, with distinctive melodic structure and chord progressions, and a propensity for improvisation over the top of the basic melody. Improvisational music is a very challenging and difficult form of

music to master, requiring extreme musical creativity and understanding of chords and harmonic structure. In an attempt to analyze the neural mechanisms and networks involved in the process of improvisation, Limb and Braun used fMRI to study a group of professional jazz pianists (Limb and Braun 2008). The six pianists were studied while using their right hand to play on a keyboard during three separate tasks: playing the C major scale in quarter notes, playing the C major scale while improvising within the scale, and listening to an audio background, and improvising on whatever notes they wanted to play. It was theorized that the last task, with the most difficult and complex improvisational activity, would have a unique neural network and activation signature. However, the activation pattern and network activity was the same between the two improvising tasks, suggesting that low-level and high-level forms are handled similarly in the brain and that the activation was due to neural activity related to creativity, and not to the complexity of the task. Most of the fMRI changes occurred in the prefrontal cortex, a region of brain involved in problem solving and providing a “sense of self.” Specifically, there was activation in the medial prefrontal cortex, an area that is important for “self-initiated” thoughts and behaviors, as well as the sensorimotor areas (see Fig. 2.9). In addition, there was suppression in the dorsolateral prefrontal cortex, which is responsible for monitoring one’s own performance, as well as deactivation of limbic structures.

The authors speculated that this neural network signature may provide a cognitive context that allows for spontaneous creative activity. Other researchers using

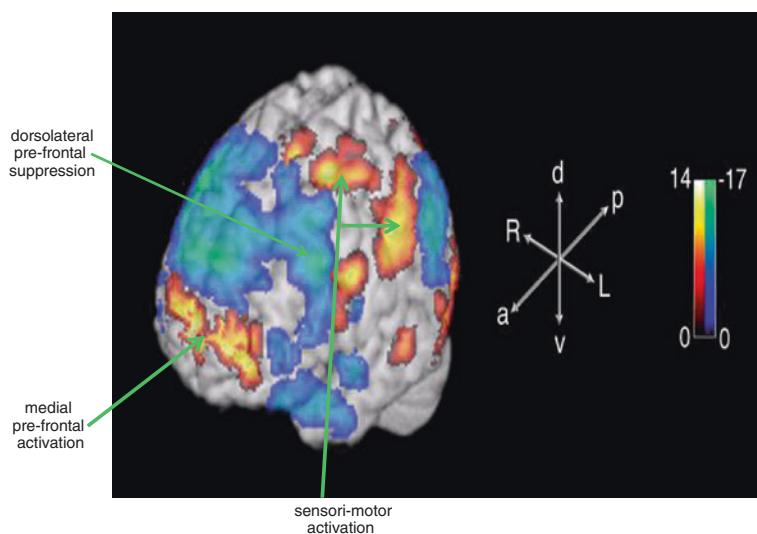


Fig. 2.9 fMRI study of a professional jazz piano player while improvising. The scan demonstrates activation in the medial prefrontal region (involved in “self-initiated” behaviors), as well as activation in the sensorimotor regions from instrumental motor activity. There is also suppression in the dorsolateral prefrontal region (involved in monitoring one’s performance). Adapted from Limb and Braun (2008), with permission from the author

fMRI techniques and different experimental musical paradigms have also implicated the prefrontal cortex, but in the context of a somewhat different neural network (Bengtsson et al. 2007; Berkowitz and Ansari 2008). Bengtsson et al. (2007) had professional pianists play under several conditions: improvise on the basis of a visually displayed melody (and memorize the notes), reproduce the improvised song from memory, or freely improvise without memorizing the performance. In an attempt to isolate the brain regions involved in musical creation, they compared and contrasted the activation patterns between the three musical conditions, as well as at rest. The activated brain network included the right dorsolateral prefrontal cortex, the presupplementary motor area, the rostral portion of the dorsal premotor cortex, and the left posterior part of the superior temporal gyrus. In their study, Berkowitz and Ansari (2008) had professional pianists improvise both rhythmic and melodic note sequences (Berkowitz and Ansari 2008). The activated brain network in this setting included the dorsal premotor cortex, rostral cingulate zone of the anterior cingulate cortex, and the inferior frontal gyrus. As the above data would suggest, there seems to be a slightly different network of brain regions that become activated and suppressed in the context of musical improvisation, depending on the tasks and experimental musical conditions required of the musicians. Further research into this important aspect of musical creativity is ongoing, but the data appear consistent in showing that the prefrontal cortex is critical in the neural network that mediates the creative musical process (López-González and Limb 2012).

2.2.6 *The “Mozart Effect” and Cognitive Aspects of Music*

There have been many claims and suggestions in the literature that exposure to music, or at least to formal musical training, can have a beneficial effect on general cognition and non-musical aspects of cognitive function (Schellenberg 2003; Rickard et al. 2005). One of the first claims of this sort was by Rauscher et al. (1993), who reported that a 10-min exposure to a Mozart Sonata was able to induce short-term increases in spatial reasoning abilities (Rauscher et al. 1993). Each participant had to perform a series of tests of spatial abilities, and before each set of tests was either exposed to the Mozart Sonata, a relaxation tape, or total silence. The performances were improved after listening to the Mozart Sonata, but not after the other two conditions, and resulted in an IQ-score improvement of approximately eight points (i.e., half a standard deviation). Because this report came out in a prestigious journal (i.e., *Nature*) and suggested a direct effect on IQ, the popular press concluded that “listening to music can make you smarter.” Critics of this research cite methodological problems that diminish the validity of the conclusions, in particular the choice of comparison conditions (Schellenberg 2003; Rickard et al. 2005).

Listening to a relaxation tape or sitting in silence does not have the same level of interest or arousal in comparison with listening to Mozart. In addition, mood is

well known to influence performance on problem-solving tasks, with superior performance associated with positive mood and affect. Therefore, the findings could have also arisen from differences in mood alteration between conditions, rather than from the exposure to Mozart *per se*. Since the initial report by Rauscher, many other investigators have attempted to replicate the study, with mixed results and using a variety of spatial tasks. In some of the positively replicated studies, other music was used instead of Mozart (e.g., Bach, Schubert). Rauscher and colleagues have replicated the study as well, with limited positive findings that are similar to the original and feel that the studies with negative results were not using the proper spatial testing tools (Rauscher et al. 1995; Rauscher and Shaw 1998). A meta-analysis of studies related to the Mozart effect, including some unpublished data, concluded that the effect was only of moderate strength, but robust (Hetland 2000). However, many critics and skeptics are inclined to believe it stems from an “arousal or mood” modulating effect (possibly dopamine-dependent?), which is predominantly a right-hemispheric function, similar to tests of complex spatial abilities (Schellenberg 2003).

The cognitive benefits of formal musical training, especially in younger children, is a much less controversial and contentious area of research (Schellenberg 2003; Rickard et al. 2005). Musical training has been associated with improvements in mathematical performance, reading ability, spatial-temporal task performance, and general IQ in elementary school-age children. For example, in one study by Schellenberg and colleagues (2004), 6-year-old children were randomly assigned to a 36-week music training program for either keyboard or voice, or assigned to a control group with either no additional lessons or drama lessons (Schellenberg 2004). Children in the keyboard music lesson group and the Kodaly voice training group showed significantly greater improvements in full-scale IQ than did the children in the two control groups. More recent longitudinal studies have also been at least partially supportive of the basic premise that musical training in childhood has positive benefits for skills related to music (e.g., fine motor skills, auditory discrimination), as well as for important skills outside the sphere of music (e.g., vocabulary, nonverbal reasoning skills) (Schlaug et al. 2005; Forgeard et al. 2008).

However, some reports have not been supportive of this concept. For example, in an Italian study of adults, 21 skilled musicians and 21 age- and education-matched non-musician controls were studied using detailed neuropsychological testing (Giovagnoli and Raglio 2011). There was no difference in the test results between the musicians and non-musicians on any of the general testing areas, including attentive, executive, linguistic, perceptual, memory, or praxic functions. Other critics of this research also cite confounding, uncontrolled variables such as higher socioeconomic status of parents, advanced resources or extracurricular activities provided by the schools, or higher prior IQ as an explanation for the effect, rather than music training. It is obvious that more detailed, long-term longitudinal studies of elementary and junior high school-age children will be necessary before we can definitively answer this important question about the effects of musical training.

2.2.7 Neurological Disorders of Music and Therapeutic Applications

Neurological dysfunction related to the inability to process or enjoy music is called amusia (Peretz 1990, 2003, 2006; Stewart et al. 2006; Alossa and Castelli 2009; García-Casares et al. 2013). Neurological disorders related to music can be grouped into three general categories: acquired amusia, congenital amusia, and musicogenic epilepsy. Acquired disorders generally arise after some form of injury to the brain, which in adults is most commonly caused by a cerebrovascular accident or stroke (Stewart et al. 2006; Peretz 2003; Alossa and Castelli 2009; García-Casares et al. 2013). Other etiologies include traumatic brain injury, surgical resection, brain hemorrhage, various forms of focal and diffuse cerebral degenerative disorders (i.e., progressive amusia), and primary or metastatic brain tumors. Over half of the cases will have associated disorders of speech perception, and about a third will also have disorders of environmental sound perception. Within the domain of music, most of the acquired disorders will affect multiple aspects of musical perception and processing (Stewart et al. 2006). However, cases have been described of very isolated musical deficits, such as loss of pitch perception, temporal processing, timbral processing, mnemonic processing, emotional processing, and loss of recognition of familiar tunes. Very-fine-grained musical dissociations have also been described in these patients, such as between pitch contour and pitch interval, and between rhythm and meter. Loss of pleasure while listening to music is one of the most common presenting complaints in patients with acquired amusia. In many of these cases, the loss of pleasure is related to abnormal musical perception, so that the music seems “mechanical,” “out of tune,” or “the instruments sound dull.” The powerful emotional responses to certain music (i.e., shivers) can also be lost after brain injury, especially damage to the medial temporal lobes and insula.

Congenital amusia refers to individuals with a lifelong inability to appreciate music and used to be referred to as “tone deaf” in the older literature (Peretz 1990, 2003, 2006; Stewart et al. 2006; Alossa and Castelli 2009; García-Casares et al. 2013; Stewart 2008). Congenital amusia appears to be a true perceptual agnosia, since the perception of music is abnormal in the presence of normal hearing and otherwise intact cognition. The main deficit seems to be in the perception and processing of pitch and pitch contour, with less consistent deficits in the perception of rhythm, temporal structure, and emotional responsiveness. Congenital amusics have severe deficits in the perception of absolute pitch, pitch direction, and pitch contour (Peretz 2003; Alossa and Castelli 2009; García-Casares et al. 2013; Stewart 2008). The most striking deficit was often in the ability to detect the proper pitch direction changes, which is critical for determining pitch contour and melody. However, this lack of processing of pitch contour related to music does not apply to the analysis of pitch changes relevant to speech (i.e., prosody). Patients may have difficulty with processing of meter and rhythm, and of “following the beat,” but this is quite variable and may be mild or severe. Similarly, the loss of emotional responsiveness to music can also be quite variable in congenital amusia. MRI studies have not demonstrated any gross structural differences

between congenital amusic and non-amusic individuals. The prevalence of congenital amusia is unknown, but is estimated to be 5 % or less. Familial cases of congenital amusia are common, and autosomal dominant inheritance with incomplete penetrance has been suggested in some cases (Stewart et al. 2006; Peretz 2003; Alossa and Castelli 2009; García-Casares et al. 2013; Stewart 2008).

Musicogenic epilepsy is defined as a type of reflex seizure disorder (i.e., precipitated by complex stimuli), in which the ictal event is induced by listening to specific songs or forms of music, often with a high emotional content (Peretz 2003; Murray 2010; Avanzini 2003; Maguire 2012). Scalp EEG recordings demonstrate focal epileptogenic discharges in the lateral and mesial temporal and orbitofrontal regions, often with a slight right-sided preponderance. The neural network responsible for linking the perception of music with the epileptogenic brain region is unknown. There is often a specific type or form of music that is peculiar to each patient as a stimulus for the epileptic event and can include certain instruments (e.g., piano, organ, church bells), types of music (e.g., rock and roll, symphonies), songs, and composers. For example, a recent case involved a 36-year-old man who reported partial seizures since the age of 24, every time he listened to emotionally charged music (Pittau et al. 2008). He underwent video-EEG recordings and fMRI while listening to “neutral” and “emotionally charged” music. During the epileptogenic music, three right temporal seizures were recorded. On fMRI, there was activation of the primary and secondary auditory cortices during the “neutral” music. However, during the “emotionally charged” musical passages, there was activation of the same auditory cortical areas, as well as widespread activation over the right frontotemporal-occipital region before onset of the seizure.

The most relevant therapeutic application of music is the field of music therapy, which has been an accepted component of Western medicine since the 1950s, but has been applied throughout the world in various forms since antiquity (Davis and Gfeller 2008; Koelsch 2009). The modern field of music therapy has been shown to be beneficial in children and adults, and for many disease states, including depression and anxiety, developmental disabilities, exercise and physical therapy, stroke recovery, tolerance of chemotherapy, and pain control (Gfeller and Thaut 2008; Thaut et al. 2008; Richardson et al. 2008; Bradt et al. 2011; Chan et al. 2011; Särkämö and Soto 2012; Clark et al. 2012). Although the exact mechanisms of the therapeutic benefit of music therapy remain unclear, it is thought to be related to the ability of music to engage multiple brain areas and neural systems within the patient, including attention, sensory processes, memory-related processes, perception-action mediation (i.e., “mirror neuron system” activity), multisensory integration, emotional processing, and the processing of musical syntax and meaning (Koelsch 2009).

2.2.8 Neurobiological Model of Music Processing and Summary

A more recent and complete model of the neural processing of music has been proposed by Koelsch and Siebel (2005) and includes several interesting and novel features (see Fig. 2.10) (Koelsch and Siebel 2005). After the musical acoustic

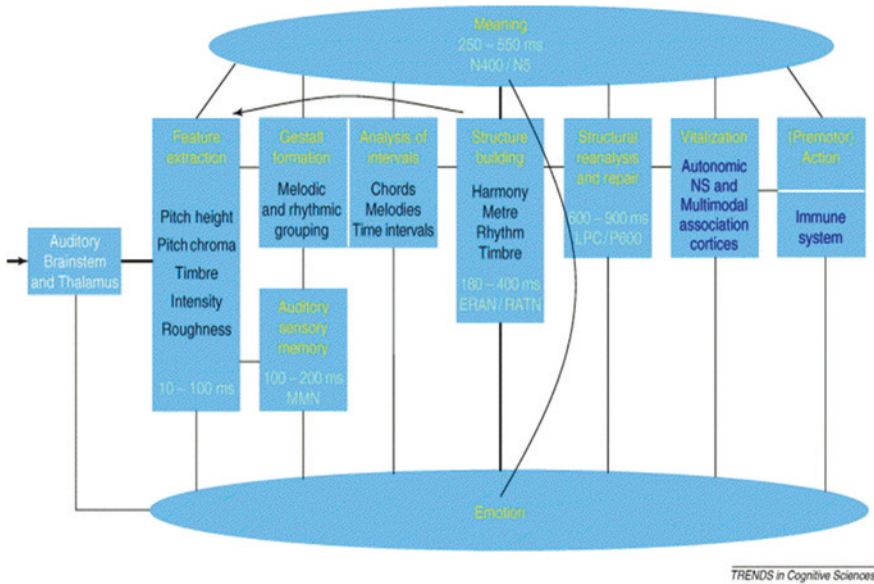


Fig. 2.10 Neurocognitive model of music perception and processing, as proposed by Koelsch and Siebel. After the musical auditory signal goes through initial auditory processing in the brainstem and thalamus, it goes through a series of compartmentalized processing steps, along with analysis for “meaning” and “emotion.” See text in Sect. 2.8 for further details. Adapted from Koelsch and Siebel (2005)

signal has passed through the middle ear and cochlea, there is preprocessing of the composite signal in the superior olivary complex and inferior colliculus for pitch, timbre, intensity, and other features. Once the signal reaches the thalamus, it is directly connected to the amygdala and medial orbitofrontal cortex, which are implicated in emotional responses and control of emotional behavior. After the thalamus, the signal is then transferred to the primary and secondary auditory cortices, where more specific musical processing occurs in regard to pitch, pitch height, timbre, sound intensity, etc.

The time course for this initial processing in the auditory cortex is estimated to be between 10 and 100 ms. After the basic auditory features have been delineated, the acoustic information enters auditory sensory memory, within a time frame of 100 and 200 ms, which is thought to be in the inferior frontolateral cortex. In parallel to this, the acoustic information also enters into a compartment the authors call Gestalt formation, where the musical signal is grouped according to basic elements of melody, rhythm, timbre, and spatial characteristics. This is important for proper grouping of the musical signal and to be able to recognize it and follow it as an “acoustic object,” with a cognitive representation. Closely linked to the stage of Gestalt formation, there is a more detailed analysis (i.e., analysis of intervals) of the acoustic signal in terms of pitch intervals, pitch directions, chords, pitch contour, melody, and temporal intervals.

Pitch contour and melody processing are predominantly mediated in the posterior part of the right STG, while processing of pitch intervals and direction involves the posterior and anterior regions of the supratemporal cortex bilaterally. The PT is also involved in the processing of pitch intervals, pitch direction, and sound sequences. After the analysis of intervals stage, on a time course of between 180 and 400 ms, there is a process of structure building, in which the musical signal goes through final processing for harmony, meter, rhythm, timbre, and temporal features. This is the process of musical syntax, where chords and harmonies are analyzed in terms of the preceding harmonic and musical context. This is a very automatic neural feature and is present in non-musicians as well as musicians, although it is developed to a much more rigorous and sophisticated level in trained musicians. Musical syntactic processing occurs predominantly in the pars opercularis of the inferior frontolateral cortex bilaterally, as well as in the anterior portion of the STG and the ventrolateral premotor cortex. In the next compartment of structural reanalysis and repair, with a time course of 600–900 ms, musical syntactic violations (e.g., abnormal chord progressions or notes out of the expected pitch contour) are determined and applied to the ongoing analysis of the acoustic signal. In parallel with the analysis of musical parameters and structure, there is an overlying process to determine “meaning” of the musical acoustic signal, with a time course of 250–550 ms.

The musical meaning could entail aspects of common forms or patterns in the music (e.g., jazz, symphonic, country, specific composers), emotional context of the music (e.g., happy, sad), social or other non-musical context (e.g., national anthem, college fight song), or meaning related to specific aspects of musical structure (e.g., unexpected chords). Similarly, from the initial phases of acoustic processing and onward, and at every stage of the model, there is input into the large bottom compartment of “emotion,” whereby the listener has to develop an emotional reaction to the musical signal, which can range from complete revulsion, to neutral apathy, to spine-tingling chills. Late in the time course of music processing is the compartment of “vitalization,” in which the body may or may not have a physical response to the music (e.g., autonomic arousal), along with cognitive integration of musical and non-musical information (e.g., emotional responses, tense, relaxed). The integration process most likely occurs in the parietal association cortices. The final compartments involve possible motor responses to the musical acoustic signal, such as tapping a finger or foot, dancing, or singing. Neuro-immunological aspects are also included, since strong emotions tied into listening to music may influence the secretion of immunoglobulins (e.g., IgA). This model is a more robust and complex approximation of the process of music perception in comparison with older models and includes novel compartments that have been overlooked in the past (e.g., gestalt formation). However, further refinements are still needed to broaden and improve the model so that it emulates the complexity of the process in the human brain.

Significant progress has been made over the past 20 years in deciphering the neural mechanisms involved in the processing of music in the brain. Most of these advancements have been driven by the availability and application of new, non-invasive neuro-imaging techniques including PET, fMRI, and MEG. Ongoing

technical refinements in these neuro-imaging modalities (e.g., stronger magnets, improved signal-to-noise ratios) will allow for even more detailed exploration of the brain and neural networks related to music. However, it is also clear from the literature cited above that even when using the exact same techniques (e.g., fMRI) and studying the same parameters (e.g., pitch, timbre), the activation patterns and associated neural networks may be similar, but often have subtle differences, as long as the investigators are using different experimental paradigms and conditions. Nonetheless, music remains a very rich avenue of exploration into the inner workings of the brain, since it involves so many different cortical and subcortical regions and neural networks. Important questions that still need to be addressed in future research include more detailed aspects of the neurobiology of musical performance, musical learning, and the process of musical composition.

In addition, further work needs to be done on the question of how the brain creates and then subsequently recognizes musical Gestalts and which neural networks mediate this activity. How does the primary and secondary auditory cortex decode and finalize processing of musical acoustic signals? How does the neural perception of music interact with the autonomic nervous system, hormonal systems, and immune system? How do the different musical processing compartments interact with each other and how does each of them interact with the musical lexicon (i.e., music-specific memory stores)? And finally, further research is needed into the various ways in which music can interact with emotion, both positive and negative. There are powerful links between specific songs in the musical lexicon and emotional responses, as well as between emotions and new music we are exposed to on a daily basis. It will be important to further clarify the neural networks and circuitry underlying the connections between powerful emotions, musical listening, and musical memories.

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