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Chapter 37

Hearing and music in dementia

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INTRODUCTION

Both music and speech are complex acoustic signals that rely on a number of brain and cognitive processes to create the sensation of hearing. The transmission of auditory signals is supported by large-scale neural networks. Changes in hearing function are generally not a major focus of concern for persons with a majority of neurodegenerative diseases associated with dementia, such as Alzheimer disease (AD). However, changes in the processing of sounds may be an early, and possibly preclinical, feature of AD and other neurodegenerative diseases. For example, patients with semantic dementia often present to a physician with difficulty comprehending speech, in addition to difficulties with finding words in conversational speech. Other persons with a dementia may have difficulty following multiple auditory streams or following complex instructions. The frequency of complaints about hearing difficulties differs by the type and stage of the neurodegenerative disease.

Persons with neurodegenerative diseases, however, rarely present with significant deficits in the processing of music, compared with persons who have an auditory agnosia or amusia, an acquired impairment in the ability to process music (see Chapters 32 and 34). In contrast, there are numerous anecdotal reports suggesting that the appreciation (and perception) of music often remains preserved in persons with AD and possibly other neurodegenerative diseases.

A key question is the extent to which the core cognitive deficits associated with various neurodegenerative diseases contribute to difficulties in comprehending auditory information versus the extent to which changes in central auditory processing may contribute to auditory comprehension difficulties. In other words, because dementia, by definition, is a progressive impairment in cognition, it is sometimes difficult to separate difficulties in sound processing due to cognitive impairment versus difficulties in sound processing due to an auditory system-specific deficit.

The aim of this chapter is to review the current state of knowledge concerning hearing and music perception in persons who have a dementia as a result of a neurodegenerative disease. The fundamental questions of this chapter are: How do persons with a neurodegenerative disease process comprehend music? Do persons with different neurodegenerative diseases perceive and process music differently? How is music used as a tool to better understand both the auditory system and neurodegenerative diseases?

OVERVIEW OF DEMENTIA

Dementia is a general term that refers to a progressive decline in cognition and behavior that impacts a person's ability to function independently in everyday life (American Psychiatric Association, 2000). Dementia is a common syndrome in older adults, and there are over 50 different causes of dementia. For the purposes of this chapter, we will focus on the most common causes of dementia (see Miller and Boeve, 2009; Ames et al., 2010; Krishnamoorthy et al., 2010 for a comprehensive overview of dementia and neurodegenerative diseases).

AD is the most common cause of dementia in adults over age 65 and accounts for approximately half of all dementia diagnoses (Alzheimer's Association, 2012). Impairment in memory is the most common cognitive and often predominant deficit in AD, but deficits in other cognitive domains (language, executive function, visuospatial skills) are often present. Other neurodegenerative diseases can also cause dementia; the most common non-AD dementias include dementia with Lewy

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bodies (DLB), frontotemporal dementia (FTD), corticobasal degeneration, progressive supranuclear palsy, and Huntington's disease. Vascular cognitive impairment (also called vascular dementia), which is caused by vascular disease in the brain, is another common cause of dementia (Rincon and Wright, 2013). Many persons with vascular dementia also have changes in the brain associated with AD. Approximately 30–60% of persons with Parkinson disease also eventually develop cognitive dysfunction (Aarsland et al., 2003; Williams-Gray et al., 2007). There is often clinical overlap between Parkinson's disease dementia and DLB.

DLB is another common cause of dementia. It is characterized by progressive cognitive and functional decline with at least two of the following additional symptoms: (1) prominent visual hallucinations; (2) fluctuations in alertness and attention; and (3) parkinsonian motor symptoms (McKeith et al., 2005). Although visual hallucinations are a prominent feature of DLB, auditory hallucinations are rare. Corticobasal degeneration and progressive supranuclear palsy are two more rare neurodegenerative diseases that are classified as atypical parkinsonian disorders (Armstrong et al., 2013; Respondek et al., 2013). Huntington's disease is another rare neurodegenerative disease that causes involuntary motor symptoms (i.e., chorea), dementia, and psychiatric symptoms (Biglan et al., 2013).

FTD is a common cause of early age-of-onset dementia (and is caused by significant atrophy in the frontal and temporal lobes of the brain. FTD can be subdivided into two language-variant syndromes (progressive non-fluent aphasia and semantic dementia) and one behavior variant, called behavioral-variant FTD (bvFTD) (Gorno-Tempini et al., 2011; Rascovsky et al., 2011). The behavioral variant of FTD is characterized by changes in personality and social behavior (e.g., impulsivity, apathy, decreased empathy, and diminished insight). Persons with semantic dementia develop a progressive loss of the meaning (semantics) for both verbal and non-verbal concepts, which is due primarily to atrophy of the temporal lobes of the brain. Persons who have progressive non-fluent aphasia develop progressive difficulty producing language (e.g., hesitant and effortful speech). Logopenic aphasia is another variant of primary progressive aphasia characterized by slow speech and naming deficits and is thought to be caused by AD (Gorno-Tempini et al., 2008).

Mild cognitive impairment (MCI) is a term used for the preclinical stage of dementia. MCI is associated with mild declines in cognitive function, but the ability to perform daily living skills is still relatively preserved. There is a high rate of progression from MCI to dementia (Petersen, 2011).

The majority of research about hearing and music in dementia has been done with persons who have AD. For this reason, the chapter will focus primarily on AD. However, the chapter will include information about hearing function and music in non-AD dementias when it is available.

HEARING FUNCTION IN NEURODEGENERATIVE DISEASES

Hearing sounds, including music, relies on both the peripheral and central auditory systems (see Chapters 1 and 2). Both the peripheral and central auditory systems undergo change with age. The section below will provide a broad overview about hearing function in aging and neurodegenerative diseases. (For further information about hearing function in aging and dementia, see Grimes, 1995 and Weinstein, 2000.)

Hearing impairment

Hearing loss is one of the most common chronic conditions in older adults (see Chapter 21). Hearing loss in the general population increases with age, and men have higher rates of hearing impairment than women. Approximately 40% of adults over age 65 have hearing loss (>30 dB loss in at least one ear), and approximately 50% of adults over age 85 have hearing loss (Gates and Mills, 2005). Age-related hearing loss (presbycusis) first affects the high-frequency range, is progressive, and can be caused by damage to either the peripheral or central auditory system (or both). Gates and Mills (2005) note that persons with hearing loss often have difficulty understanding conversations and misperceive phonetically similar words, such as "map" and "mat." Family members or friends are often more aware of the change in hearing function than the older person with hearing loss. Hearing loss in older adults can also affect the ability to perceive and comprehend music, but few studies have explored this topic.

A number of studies have examined the relationship between hearing loss and cognitive decline in older adults. Gennis and colleagues (1991) reviewed 15 studies and concluded that hearing loss was more common in persons with dementia, but there was considerable heterogeneity in the study designs, and the underlying causes of the dementia were not always clear. Other studies suggest that the hearing loss in persons with dementia is more severe than older adults without cognitive decline (Uhlmann et al., 1989; Lin et al., 2011). Recent studies also suggest that adults with hearing loss are more likely to develop AD or other dementias over time. For example, Lin and colleagues (2013) found that hearing loss (pure-tone average >25 dB) was independently associated with both increased rate of cognitive decline and incident cognitive impairment in a large sample of community-dwelling older adults.

Several recent studies suggest that adults with Parkinson's disease may have a higher prevalence of age-related, high-frequency sensorineural hearing loss relative to healthy adults. One recent study involving 118 patients with Parkinson's disease found a higher prevalence of age-dependent high-frequency hearing loss than age- and sex-matched controls (Vitale et al., 2012). Within this cohort, 26% had mild, 63% had moderate, and 11% had severe hearing loss. The Parkinson's disease patients with hearing impairment were older, more likely to be male, and had a later age at onset than the Parkinson's disease patients with normal hearing. The authors also noted that the Parkinson's disease patients were generally unaware of their hearing loss.

It is also important to remember that the patient with dementia may not complain of hearing loss symptoms. Gates and Mills (2005) recommended an examination of hearing function in any person with cognitive decline. They also note that tinnitus is a common comorbid condition with hearing loss and should be queried in persons with cognitive decline. It is possible that hearing loss symptoms are underreported in persons with neurodegenerative diseases, as they may be regarded as secondary to concerns about memory or are confused as memory or communication symptoms. It is also possible that dementia may be overdiagnosed in persons with hearing loss.

Peripheral auditory system function

Persons with a neurodegenerative disease (with the diagnoses discussed above) are generally thought to have an intact peripheral auditory system and are only affected by typical, age-related changes. That is, most neurodegenerative diseases do not directly damage the peripheral auditory system. Autopsy studies have not detected neuropathologic changes associated with AD in the peripheral auditory system (Sinha et al., 1993). However, only a few studies have been done, and the majority of these autopsy studies focus on AD. The peripheral auditory system is just beginning to be studied in non-AD dementias.

Early studies documented normal peripheral hearing function in AD patients (Grimes et al., 1985; Eustache et al., 1995; Gates et al., 1995). For example, Kurylo and colleagues (1993) investigated a comprehensive battery of auditory function, including pure-tone thresholds, sound localization, pitch perception of complex tones, phoneme perception, timbre discrimination, and tonal memory (from the Seashore Tests of Musical Abilities). There were no differences between patients with AD and matched older adults on the majority of these tests. Another study (Strouse et al., 1995) administered immittance tests (e.g., tympanograms, acoustic reflex thresholds), pure-tone and speech audiometric testing, word recognition, and distortion product otoacoustic emissions testing to 10 mild to moderate patients with AD and matched controls. They found that the AD patients had only slightly worse low-frequency thresholds compared to the controls. Another study involving 33 patients with a diagnosis of AD, progressive nonfluent aphasia, or logopenic aphasia found only small differences on sound detection thresholds in the patient groups compared to controls (Goll et al., 2011). Mahoney and colleagues (2011) reported that 32% of patients with semantic dementia complained of tinnitus or hyperacusis, but peripheral hearing function was not examined.

A few other less common adult-onset neurodegenerative diseases occasionally involve the peripheral auditory system. For example, one study documented a 71-year-old man who developed a rapidly progressive dementia with features of DLB and also inflammation of the cartilage of the pinna (Head et al., 2006). An autopsy revealed inflammation-induced neurodegeneration caused by relapsing polychondritis, an autoimmune inflammatory disorder of cartilaginous tissues. There are also a few other rare neurodegenerative diseases or genetic mutations that can cause a dementia and sensorineural hearing loss (e.g., mitochondrial disease syndromes, adult-onset Friedreich's ataxia). A few recent studies have focused on cases of autosomal-dominant hereditary sensory and autonomic neuropathy with dementia and hearing loss (HSAN1) (Wright and Dyck, 1995). Klein and colleagues (2011, 2013; U.S. Congress, Office of Technology Assessment, 1992) described a primarily adult-onset hearing loss and neuropathy followed by memory decline or personality changes typical of FTD in the 30s and 40s with a mutation in DNA methyltransferase 1 (DNMT1). Autopsies in persons with a DNMT1 mutation in a case series from Japan revealed diffuse non-specific degeneration and glial activation especially in the frontal, temporal, parietal, and occipital cortex, hippocampus, and thalamus, but the auditory system was not mentioned (Hojo et al., 2004).

Central auditory system

Because neurodegenerative diseases primarily affect the central nervous system, the majority of studies have focused on the central auditory system. The changes to the central auditory system are thought to occur as a result of the neurodegenerative diseases, in addition to age-related changes in the central auditory system. Histopathologic and morphometric studies have found a number of neuropathologic changes in the central auditory system in different neurodegenerative diseases. The auditory system has been most extensively studied in persons with AD. Neuron loss, neuritic plaques, and neurofibrillary tangles, the classic neuropathologic lesions of AD, have been identified in auditory system brainstem and midbrain nuclei, including the olivary nucleus, inferior colliculus, and medial geniculate body (Ohm and Braak, 1989; Dugger et al., 2011). In addition, plaques and tangles are also common in primary auditory and auditory association cortex in persons with AD (Sinha et al., 1993; Chance et al., 2011). Neuropathologic studies of the central auditory system are less common in non-AD dementias. A few studies suggest that an accumulation of tau neuropathology in auditory brainstem nuclei in persons with progressive supranuclear palsy (Dugger et al., 2011) and severe neuronal loss has been documented in the auditory cortex of persons with FTD and primary progressive aphasia (Baloyannis et al., 2011). These neuropathologic changes of the central auditory system are thought to be related to the processing of sounds.

The majority of studies focus on the processing of verbal information, while studies about the processing of non-verbal information, including music and environmental sounds, are less commonly done. This section will provide a brief overview of central auditory system dysfunction in neurodegenerative diseases, and additional information about the processing of music and other non-verbal sounds will be discussed in the following two sections.

Early studies in the 1980s used dichotic listening paradigms (simultaneous presentation of different acoustic signals to the right and left ears) and other basic auditory perceptual tasks to study central auditory function in persons with AD. For example, Grimes and colleagues (1985) found that 81% of the patients with AD had abnormal scores on dichotic listening tasks. The dichotic listening scores correlated with performance on tests of cognition, volume of the temporal lobes on brain computed tomography imaging, and metabolism of the left temporal lobe using positron emission tomography imaging. That is, lower scores on dichotic listening tasks correlated with lower cognitive scores, less brain volume, and lower metabolism in the left temporal lobe. Other early studies using dichotic listening methods also documented auditory processing impairments in AD patients (Grady et al., 1989; Mohr et al., 1990).

Persons with MCI may also have central auditory function impairments. For example, Gates and colleagues (2008) examined central auditory processing using a comprehensive battery (synthetic sentence identification with ipsilateral competing message, dichotic sentence identification, and dichotic digits) in a large cohort of older adults who had mild memory impairment (but not demented) or dementia based on a cognitive screening test (Cognitive Ability Screening Instrument). The authors found that the persons with mild memory impairment performed worse than matched controls but better than the demented patients, even after controlling for age, hearing threshold, and word recognition scores. However, the underlying diagnoses of the demented participants were not reported. Another study also found that persons with MCI had an impairment on a dichotic listening task that was intermediate between healthy adults and AD patients (Idrizbegovic et al., 2011), again suggesting that deficits in central auditory processing occur before the onset of dementia and get worse after the onset of dementia symptoms.

Impairments in central auditory function may also be a risk for developing dementia. For example, one study recently found that older adults with severe central auditory dysfunction, particularly as measured by the Dichotic Sentence Identification test, were at increased risk for developing incident AD after 3 years (Gates et al., 2011). The majority of those who developed AD also had lower memory scores, as measured by the memory subscale of the Cognitive Abilities Screening Instrument. As discussed above, another recent study found that hearing loss (pure-tone average >25 dB) was independently associated with increased rate of cognitive decline and incident cognitive impairment in a large sample of community-dwelling older adults (Lin et al., 2013).

Some authors propose to frame auditory cognition deficits in terms of "auditory objects" or "auditory scene analysis," the ability to parse sound sources in the auditory environment (Goll et al., 2010b). For example, Goll and colleagues (2012a) recently assessed auditory scene analysis of both verbal and non-verbal sounds in a cohort of 21 persons with AD. The persons with AD performed much worse than matched controls on both auditory scene analysis tasks, but their performance was somewhat attenuated after accounting for visuospatial working memory. They also found that performance correlated with brain volume in several posterior cortical areas, using voxel-based morphometry of brain magnetic resonance imaging (MRI).

Central auditory processing deficits have also been studied in a few non-AD dementias. For example, Goll and colleagues (2010a) found significant difficulties in the processing of complex non-verbal sounds in 12 patients with progressive non-fluent aphasia and 8 patients with semantic dementia. The authors used several newly designed auditory tasks to assess early perceptual, apperceptive, and semantic levels of non-verbal auditory processing. While patients with progressive non-fluent aphasia were particularly impaired on the early perceptual tasks, the semantic dementia patients had particular difficulty with the processing of semantic aspects of non-verbal sounds.

In conclusion, impairments in the central auditory system are common in persons with various neurodegenerative diseases. However, the majority of studies have focused on AD, while an interest in studying central auditory function in non-AD dementias is increasing. Additional consideration of the central auditory system processing of music and non-verbal sounds can be found in the next two sections.

PROCESSING OF MUSIC IN NEURODEGENERATIVE DISEASES

As discussed in the introduction, persons with neurodegenerative diseases rarely present with significant deficits in the processing of music, compared with persons who have an auditory agnosia or amusia, an acquired impairment in the ability to process music (see Chapters 32 and 34). In contrast, there are numerous anecdotal reports suggesting that the appreciation (and perception) of music often remains preserved in persons with AD and possibly other neurodegenerative diseases. How do persons with a neurodegenerative disease process and comprehend music? Do persons with different neurodegenerative diseases perceive and process music differently? How is music used as a tool to better understand both the auditory system and neurodegenerative diseases?

Framework for examining music perception in neurodegenerative diseases

As discussed in Chapter 11, there are both perceptual and associative aspects involved in the perception of music. Basic-level perceptual hearing processes extract pitch, rhythm, timbre, and timing information, while higher-order cognitive processes help store and associate music sequences with long-term memories. All of these processes facilitate recognition of a musical sequence as meaningful or familiar.

One of the early music psychologists, Carl Seashore (1866–1949), provided a useful framework for understanding how the physical aspects of sound (frequency, intensity, duration, and waveform) are mapped on to the perceptual qualities of music (pitch, loudness, time, timbre). That is, the acoustic aspect of frequency (number of waves per second) is associated with the perception of pitch; intensity (decibels) is associated with loudness; duration (time intervals) is associated with time/meter; and wave form (tone quality from pure tone to noise) is associated with the perception of timbre. These basic physical components of musical sounds can be combined to create music intervals, scales, harmonies, melodies, and musical compositions. Figure 37.1 depicts a commonly used contemporary cognitive model of music recognition, as proposed by Peretz and Coltheart (2003). Each box represents a music-processing component, while the lines between boxes designate the path of

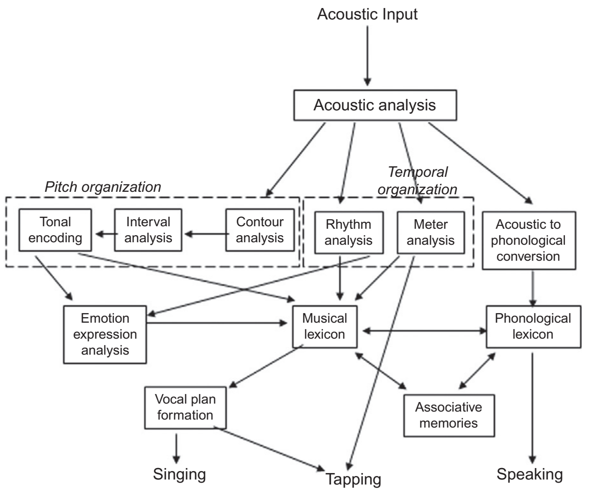

Fig. 37.1. Cognitive model of music processing. Each box represents a processing component, and arrows represent pathways of information flow or communication between processing components. A neurologic anomaly may either damage a processing component (box) or interfere with the flow of information between two boxes. All components whose domains appear to be specific to music are in green; others are in blue. There are three neurally individuated components in italics – rhythm analysis, meter analysis, and emotion expression analysis – whose specificity to music is currently unknown. They are represented here in blue, but future work may provide evidence for representing them in green. (Reproduced from Peretz and Coltheart, 2003, with permission.)

information processing between components. The acoustic signal enters from the top of the model. In addition, Stewart and colleagues (2006) identified the most important brain areas implicated in disorders of music listening. The schematic of the brain at the top provides the anatomic areas involved in music listening, while the four schematics below identify specific aspects of music processing. The authors argue that this framework can be applied to both acquired and congenital disorders of music listening. It is important to keep in mind that this framework was developed from studies of patients with focal brain lesions (e.g., stroke); however, there are no compelling reasons to think that the deficits in music processing observed in persons with dementia would not follow this framework (Fig. 37.2).

The melody is often the most conspicuous aspect of music, and many studies focus on the processing of familiar and unfamiliar melodies. For familiar melodies in western cultures, healthy adults store relatively precise knowledge about the notes and timing that comprise the melody. Recognition of a melody as familiar depends on the ability to match the mental representation/percept of the melody with a "musical lexicon," which includes all melodies known to the listener (Peretz and Coltheart, 2003). Recognition of familiar

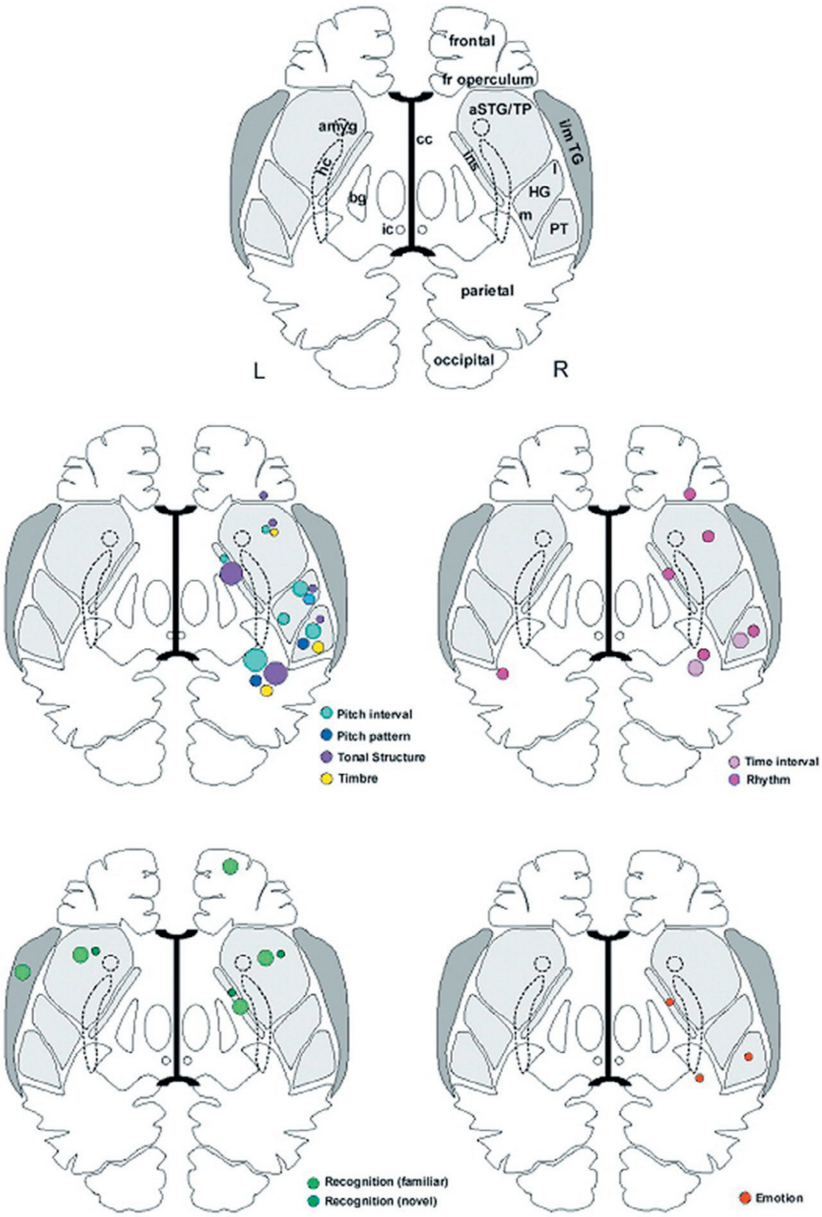

Fig. 37.2. Brain areas implicated in disorders of music listening. Critical brain substrates for musical-listening disorders across studies. Five cartoons are shown, each depicting the brain in a schematic axial section that includes all key anatomic areas involved in music listening (identified on the top cartoon); the corpus callosum (black), superior temporal plane (light gray), and middle/inferior temporal gyri (dark gray areas, in exploded view) are colored for ease of identification. Musical functions analyzed in Supplementary Table 1 (http://brain.oxfordjournals.org/content/129/10/2533.figures-only) have been grouped as follows: pitch processing (pitch interval, pitch pattern, tonal structure, timbre); temporal processing (time interval, rhythm); musical memory (familiar and novel material); and emotional response to music. Each group of functions is assigned to a separate cartoon; individual functions are identified to the right of the corresponding cartoon. Raw data from Supplementary Table 1 have been thresholded; the presence of a colored circle corresponding to a particular function in a region indicates that at least 50% of studies of the function implicate that region. The size of each circle is scaled according to the proportion of studies of the function implicating that region (see text). Meter is not represented as no brain area was implicated in 50% or more of cases. amyg, amygdala; aSTG, anterior superior temporal gyrus; bg, basal ganglia; cc, corpus callosum; r, frontal; hc, hippocampal; HG, Heschl's gyrus; ic, inferior colliculi; i, inferior; ins, insula; l, lateral; m, medial; thal, thalamus; PT, planum temporale; TG, temporal gyrus. (Reproduced from Stewart et al., 2006, with permission.)

music can be assessed using a variety of methods. Several studies asked participants to judge the familiarity of a melody to determine if the listener can discriminate familiar and novel melodies. Another method is to ask participants to listen to a melody and determine if the melody is correctly played or has an error (e.g., pitch, rhythm). The Distorted Tunes Test (Drayna et al., 2001) is one example of a pitch error detection task. Brattico and colleagues (2006) suggest that the identification of errors in melodies occurs rapidly and automatically, even with unfamiliar melodies. Several studies also ask participants to generate a title for a familiar melody, but this type of task requires different cognitive processes (e.g., verbal recall) compared with recognizing melodies with errors. The processing of unfamiliar melodies can be assessed using a number of different paradigms. For example, both the explicit and implicit memory of unfamiliar melodies can be examined. The Montreal Battery for Evaluation of Amusia (Peretz et al., 2003) includes several tasks that require comparisons of unfamiliar melodies that may differ by notes, contour, or rhythmic patterns.

The next sections will review the current literature about how music, and melodies in particular, is processed in persons who have a neurodegenerative disease. It is important to keep in mind that performance on various music tasks can be affected by the type and severity of dementia. This often makes comparisons across studies difficult. Performance on music tasks can also be affected by the amount of prior music training. The majority of case studies reviewed below focus on persons who are either professional or amateur musicians, while many of the group studies include persons with different levels of music background. Not all studies report the music background of the participants. Similar to the studies reviewed above, the majority of studies about music have been done with persons with AD. However, recent studies focus more on the processing of music in non-AD dementias.

Alzheimer disease

As mentioned in the introduction of this chapter, there are several case reports in the literature that document a relative preservation of music abilities in persons with AD. These reports primarily focus on the preserved ability to continue playing a musical instrument after the onset of dementia. Table 37.1 summarizes these case studies and provides a short summary of the findings. In several of the early case studies, Beatty and colleagues described the preserved music abilities of persons with AD who had music training (Beatty, 1988, 1999; Beatty et al., 1994, 1999; Beatty and Greiner, 1998; Cowles et al., 2003). For example, patient T was a 71-year-old amateur trombone player who continued to play in a Dixieland jazz band after he developed dementia (later confirmed to be AD by autopsy) (Beatty et al., 1994, 1997). When patient T was in the mild stages of dementia (with a Mini-Mental State Examination score of 20 out of 30), the authors made videotaped recordings of his playing during a band performance and asked raters to compare the quality of his playing at that time with recordings of him playing from approximately 30 years prior. The raters judged these two playing examples as equivalent, suggesting that there had not been any significant decline in his playing ability after the onset of dementia. Patient T was also asked to listen to 20 familiar holiday songs and generate the titles. He recalled 80% of the song titles, but his performance was slightly below a group of healthy controls who recalled 95% of the titles. In another early case report, Crystal and colleagues (Beatty and Greiner, 1998) described an 82-year-old music editor and pianist who was evaluated during the MCI stage of AD. At that time, he was able to play, from memory, 13 popular classic music compositions. However, 3 years later, he was only able to play a few bars of the same pieces. Several more recent case studies have examined both music perception and production in more detail, including comparisons with non-AD dementias (Cuddy and Duffin, 2005; Hailstone et al., 2009; Vanstone et al., 2009; Omar et al., 2010; Weinstein et al., 2011). Polk and Kertesz (1993) studied two persons with atypical presentations of AD (i.e., progressive aphasia and posterior cortical atrophy).

After the early case studies in the 1980s, the examination of music skills in persons with dementia eventually expanded. Subsequent research aimed to better understand how music is processed by persons with AD, and eventually, other types of neurodegenerative diseases. In addition, a number of group studies were conducted.

Several studies have focused on the ability of persons with AD to process both familiar and unfamiliar melodies. Persons with AD are generally able to distinguish melodies as familiar or unfamiliar (familiarity decision). This is often assessed by asking participants to listen to a melodic excerpt and decide if the excerpt is familiar or novel (new) or old. The findings with AD patients, however, are somewhat mixed. In one study, the persons with AD performed slightly lower than healthy controls (Bartlett et al., 1995) when asked to discriminate familiar and unfamiliar melodies, while other studies found no differences between AD patients and controls (Cuddy and Duffin, 2005; Hsieh et al., 2011). However, persons with AD may have difficulty with the explicit recognition of familiar melodies. One study presented eight familiar melodies and then asked 15 persons with mild to moderately severe AD to if the melodies in the next set were old

Table 37.1

Summary of case studies investigating music in persons with dementia

Study	Case	Background	Diagnosis	Main findings
Beatty et al. (1988)	GW	Music teacher and pianist	AD	Preserved ability to play piano; impaired ability to name familiar music
Crystal et al. (1989)	–	82-year-old music editor and pianist	MCI due to AD	Preserved ability to play piano; unable to name title or composers
Polk and Kertesz (1993)	CW	58-year-old guitar teacher	Primary progressive aphasia due to AD	Preserved ability to play guitar and recognize familiar melodies; unable to reproduce rhythms
Polk and Kertesz, (1993)	MA	53-year-old piano teacher	Posterior cortical atrophy due to AD	Preserved ability to name familiar tunes, discriminate melodies, identify pitch errors, and reproduce rhythmic patterns; impaired ability to play piano
Beatty et al. (1994) Beatty et al. (1997)	T	71-year-old amateur trombonist	AD (pathologically confirmed)	Preserved ability to play trombone and name familiar tunes
Johnson and Ulatowska (1996)	DN	76-year-old non-musician	AD	Preserved ability to reproduce melodies and rhythmic patterns and sing familiar songs, which declined over 2 years
Beatty et al. (1999)	ML	79-year-old amateur pianist	AD	Preserved ability to play piano; difficulty learning new song and impaired naming of familiar tunes and rhythm recognition
Miller et al. (2000)	4	49-year-old non-musician	Primary progressive aphasia	Compulsive whistling; composed songs about his bird
Miller et al. (2000)	5	78-year-old non-musician	Primary progressive aphasia	New skill in composing classic music
Miller et al. (2000)	6	71-year-old musician	Primary progressive aphasia	Composed songs that captured personalities of his acquaintances
Tzortzis et al. (2000)	MM	74-year-old pianist and composer	Primary progressive aphasia	Preserved ability to compose and play piano. Impaired naming of nonmusical stimuli, but preserved naming of musical instrument sounds
Cowles et al. (2003)	CL	80-year-old amateur violinist and pianist	AD	Learned to play new song on violin; preserved ability to play previously known tunes on violin and piano, recognize familiar songs, and reproduce rhythmic patterns
Cuddy and Duffin (2005) Vanstone et al. (2009)	EN	84-year-old amateur pianist	AD (pathologically confirmed)	Generally preserved ability to recognize familiar music
Fornazzari et al. (2006)	–	63-year-old professional pianist	AD	Preserved ability to read, interpret, and learn new musical pieces
Hailstone et al. (2009)	–	56-year-old non-musician	Semantic dementia	Correctly sang 63% of familiar melodies; increased interest in music listening and singing along
Matthews et al. (2009)	JS	30-year-old non-musician	Auditory agnosia due to neurodegenerative disease	Preserved affective response when listening to personal music; impaired performance on majority of music-processing tasks administered
Vanstone et al. (2009)	VC	83-year-old amateur pianist	AD	Preserved ability to recognize and sing familiar tunes; diminished ability to play piano
Barquero et al. (2010)	–	53-year-old music critic	Frontotemporal dementia (pathologically confirmed)	Preserved ability to recognize familiar tunes and process rhythm and music emotions;

Table 37.1

Continued

Study	Case	Background	Diagnosis	Main findings
				impaired ability to judge quality of music performance
Omar et al. (2010)	BR	56-year-old professional trumpet player	Semantic dementia	Preserved recognition of music and music symbols; impaired recognition of music emotions and recognition of musical instruments
Omar et al. (2010)	WW	67-year-old music librarian and oboist	AD	Preserved recognition of music emotions and musical instruments; impaired recognition of music and music symbols
Weinstein et al. (2011)	–	59-year-old harpsichordist	Semantic dementia	Preserved ability to play harpsichord and learn new complex pieces

AD, Alzheimer disease; MCI, mild cognitive impairment.

or new (Bartlett et al., 1995) AD patients performed worse than matched controls, suggesting that the explicit memory for familiar melodies may not remain preserved in AD. Hsieh and colleagues (2011) found that the recognition of familiar tunes correlated with the volume of the right anterior temporal lobe.

Persons with AD appear to retain the ability to recognize pitch or rhythmic errors in familiar tunes (e.g., wrong notes). For example, patient EN, who was in the severe stages of AD (Mini-Mental State Examination score of 8), was able to correctly identify familiar melodies with wrong notes (pitch errors) for 25 out of 26 tunes (Cuddy and Duffin, 2005). In another group study, Johnson and colleagues (2011) examined the ability of mildly demented patients with AD to detect pitch errors in highly familiar melodies. The AD patients performed similarly to matched controls, and, as expected, the key-violating pitch errors were easier to detect than key-preserving pitch errors for both groups. Performance on this familiar melody pitch detection task correlated with gray-matter volume in the right temporal cortex, as measured by voxel-based morphometry analysis of brain MRI. Another recent study found variability (ranging from 35% to 100% correct) in the ability of moderate to severely impaired AD patients to detect errors in familiar tunes (Vanstone and Cuddy, 2010).

Several studies have evaluated the ability of persons with AD to generate a title for familiar tune (i.e., name that tune) as another way to assess knowledge about familiar melodies. As discussed above, generating a title for a familiar melody requires a different type of cognitive process (e.g., verbal recall) compared with recognizing melodies with errors. After listening to an excerpt from a familiar melody, participants are asked to generate the title or select the correct title in a multiple-choice format. While some studies found that AD patients were able to generate a similar number of titles as controls (Hsieh et al., 2012), the majority of studies found that AD patients generated fewer song titles for familiar tunes than healthy controls (Crystal et al., 1989; Bartlett et al., 1995; Cuddy and Duffin, 2005), including several case studies of musicians with AD (Beatty et al., 1994; Cowles et al., 2003; Omar et al., 2010). However, when given a multiple-choice format, the AD patients may be able to improve their score to the level of the controls (Cowles et al., 2003; Johnson et al., 2011), suggesting that the knowledge about the tunes may be intact but the ability to access the verbal labels (titles) may be impaired.

It also appears that AD patients are generally able to discriminate two short, unfamiliar melodic excerpts that may differ in a number of melodic aspects, such as pitch or rhythm. For example, two studies used the Scale subtest from the Montreal Battery for the Evaluation of Amusia, which asks participants to listen to two unfamiliar melodies and determine if the second melody was the same as or different from the first melody. Half of the second melodies in the Scale subtest have an alteration of one pitch (note). Both studies found that mildly demented AD patients performed similarly to healthy controls, suggesting that AD patients are able to process novel melodic information that is presented in relatively brief formats (Hsieh et al., 2011; Johnson et al., 2011). Omar and colleagues (2010) examined other aspects of unfamiliar melody processing in their case report of WW, who scored below controls on tasks that required the processing of interval and timbre in unfamiliar melodies. In contrast, WW was able to discriminate unfamiliar melodies that differed by alterations in scale, contour, and rhythm.

In several other studies, the explicit short-term memory for unfamiliar melodies was examined in persons with AD. One study required participants to listen to eight unfamiliar melodies (presented twice) and then make old/new judgments about a new set of melodies (half of which were novel) (Halpern and O'Connor, 2000). Persons with AD performed similarly to controls, but worse than younger adults, on the explicit music memory task. However, both AD and age-matched controls performed near chance. Two other studies found that AD patients scored lower than controls on a task requiring explicit memory for unfamiliar melodies (Bartlett et al., 1995; Quoniam et al., 2003). Implicit memory for unfamiliar melodies may also be impaired in persons with AD. Implicit memory for unfamiliar music was examined by asking persons with AD to listen to unfamiliar melodies over several trials and rate their preference, with the idea that preference ratings increase after more exposure to the melodies ("mere exposure effect"). One study found that the preference ratings increased with the number of presentations for AD patients (Quoniam et al., 2003), while another study did not find this pattern (Halpern and O'Connor, 2000). The studies included patients with different dementia severity, and the tasks were slightly different, so it is difficult to make comparisons.

Other aspects of music processing, such as pitch discrimination, recognition of major versus minor tonality (e.g., scale, chords), timbre and meter perception, are rarely examined in detail. However, a few studies suggest that the the processing of basic music components may remain relatively intact in persons with AD. For example, several studies report intact pitch discrimination (Johnson et al., 2011; Goll et al., 2012a), meter perception (Cowles et al., 2003), tonality discrimination (Mohr et al., 1990), and timbre perception (Goll et al., 2010b).

Only a few studies have examined the auditory processing of rhythmic information in music with persons with AD. Two case studies administered a modified version of the Seashore Rhythm subtest from the Seashore Test of Musical Talent. Both ML and SL were able to complete this task, which requires participants to judge whether two rhythmic patterns are the same or different (Beatty et al., 1999; Cowles et al., 2003). The recognition of meter (waltz vs march) was intact in patient SL (Cowles et al., 2003). However, additional studies are needed to make more general conclusions about rhythm perception in persons with AD.

There are a few case reports documenting the ability of persons with AD to learn new music. One case report described an 80-year-old amateur violinist (SL) with moderately severe AD who was able to learn a new, moderately difficult violin composition over six sessions over 2 months (Cowles et al., 2003). Raters judged the quality of his violin playing as "slightly better than that of a good high school violinist." Another reported that a professional pianist in the severe stages of AD was able to learn and recall a new eight-bar composition (Fornazzari et al., 2006). However, reports like these are quite rare, and it is not yet known if the ability to learn a new musical composition is common in more than just a few exceptional cases of AD.

There has been a recent interest in studying "auditory objects" in persons with dementia. Auditory objects can be defined as a "collection of acoustic data bound in a common perceptual representation an disambiguated from the auditory scene" (p. 617) (Goll et al., 2010b) These studies often consider basic levels of musical sound processing in addition to higher levels of sound conceptualization. For example, Goll and colleagues (2011) completed a systematic study of non-verbal sound processing, including music, in 21 persons with AD (and other neurodegenerative diseases, also discussed below). They found that AD patients scored lower than controls on timbre and pitch perception; however, after adjusting for performance on a spatial working-memory task, the AD patients performed similarly to controls. As discussed below, patients with progressive non-fluent aphasia and logopenic aphasia had difficulty with timbre perception. In contrast, the AD patients had a disproportionate impairment on a task that required recognition of degraded sounds based on perceptual rather than semantic information, even after adjustment for spatial working-memory performance. On this task, participants were asked to decide whether a degraded sound was more like an animal calling or a tool being used.

Frontotemporal dementia

Although the initial studies about music and dementia focused on persons with AD, more recent studies have examined music abilities in persons with non-AD dementias, including the variants of FTD. Several case studies of persons with semantic dementia have recently been published. For example, a 56-year-old professional trumpet player and music teacher (BR) completed an extensive battery of tests to examine his music abilities after developing semantic dementia (Omar et al., 2010). On tests of music perception (from the Montreal Battery for the Evaluation of Amusia), he scored lower than controls on the recognition of melodic contour (shape of the melody), intervals, and timbre. He also had difficulty recognizing emotions in music and identifying the sounds of musical instruments. He was, however, able to play familiar pieces from memory after music cueing and continued to play his trumpet (non-professionally). As another example, a 64-year-old semiprofessional harpsichordist diagnosed with semantic dementia was able to perform technically demanding compositions and generate appropriate stylistic embellishments 5 years after the onset of semantic dementia (Weinstein et al., 2011). However, additional tests of music perception were not administered with the harpsichordist.

There have also been a few group studies involving patients with semantic dementia (who are mostly non-musicians). These studies suggest that, while several aspects of music knowledge can remain preserved in semantic dementia, they may have difficulty processing familiar melodies. When examining the recognition of familiar melodies, two studies found that patients with semantic dementia had difficulty in either detecting "wrong notes" (pitch errors) in familiar tunes or judging if a tune was familiar or novel (Hsieh et al., 2011; Johnson et al., 2011). Patients with semantic dementia also had significant difficulty generating titles for familiar melodies or selecting the famous title from a four-item multiple-choice format. However, Omar and colleagues (2010) found that their 56-year-old trumpet player with semantic dementia could match titles to several famous melodies. It is important to keep in mind, however, that the majority of case studies involve persons who have a background in music, while most of the group studies involve non-musicians with varying degrees of involvement in music.

Several other studies have documented an increased interest in music after developing semantic dementia (Miller et al., 2000; Boeve and Geda, 2001; Hailstone et al., 2009) and a change in music taste (new interest in pop music) in a person with FTD (Geroldi et al., 2000). Barquero and colleagues (2010) studied a 53-year-old music critic whose first symptom was a complaint about trouble evaluating the "quality of a musical performance." Although her neurologic and neuropsychologic examinations were normal, she had difficulty differentiating renditions of music performed by either a professional or a beginner music student. It appears that her ability to recognize various music elements (e.g., melodies, pitch errors, rhythm, and meter) was preserved at that time, although the specific tasks and results are not available. She later developed a progressive dementia syndrome and was diagnosed with FTD caused by a novel progranulin mutation. An autopsy revealed ubiquitin-positive inclusions, particularly in the frontal, temporal, and parietal cortices.

A few studies have focused on persons with progressive aphasia. For example, Miller and colleagues (2000) studied three individuals with progressive language symptoms (variants of primary progressive aphasia). One non-musician developed compulsive whistling and composed songs about a bird, and the other non-musician began composing classic music that was performed in public (despite the lack of prior training in music composition). The third patient was a skilled musician who also composed songs. Tzortzis and colleagues (2000) performed a comprehensive examination of music abilities of a professional pianist and composer with a 9-year history of progressive aphasia. They administered a series of tests that focused on receptive music skills (e.g., pitch error detection, identification of chords and musical styles) and expressive music skills (e.g., playing music from memory, reading an unfamiliar musical score). They found a consistent preservation of both receptive and expressive music skills, and the patient continued to compose music. The famous French composer, Maurice Ravel, is another example of a musician who developed a progressive aphasia and apraxia but was able to compose for a time after the onset of symptoms (Amaducci et al., 2002). The progression symptoms, however, eventually affected his ability to compose, although Ravel reported that he could "hear" the music in his head. Additional studies are needed to better understand the effect of progressive aphasia on music skills.

Parkinson's disease

Only a few studies to date have focused on the perception of music in persons with Parkinson's disease. Most studies have focused on rhythmic auditory cueing (using music) to improve gait in Parkinson's disease (e.g., Thaut et al., 2001). One study examined rhythm discrimination in 15 persons with Parkinson's disease (with Hoehn and Yahr stages 1 or 2) (Grahn and Brett, 2009). The authors administered a series of rhythm recognition tasks with and without a clear beat. The results suggested that the patients with Parkinson's disease had difficulty perceiving the beat structure, compared with matched controls. However, the patients performed similarly to controls in the non-beat conditions. Another study found that patients with Parkinson's disease had difficulty recognizing fear and anger in music (van Tricht et al., 2010). In this study, participants were asked to listen to 32 music excerpts and determine whether they expressed happiness, sadness, fear, or anger. Interestingly, the persons with Parkinson's disease were able to correctly identify happiness and sadness in the music but had more difficulty identifying anger and fear (Fig. 37.3). The authors argued that the patients did not have deficits in the processing of music, as they performed similarly to controls on two subtests from the Montreal Battery for the Evaluation of Amusia (i.e., melodies, rhythm). The difficulty identifying fear and anger in music was consistent with other studies suggesting that persons with Parkinson's disease have difficulty recognizing emotions.

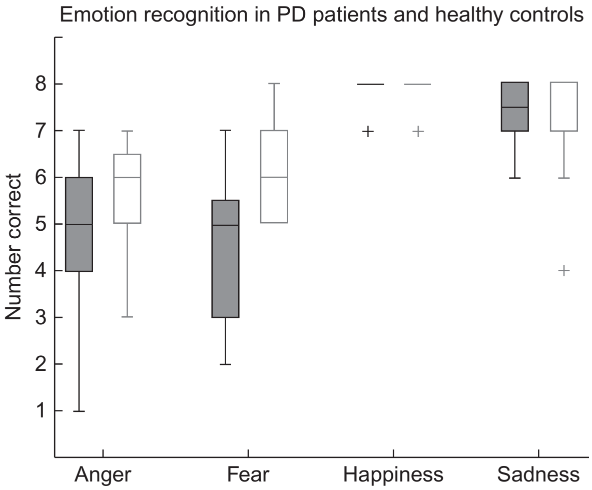

Fig. 37.3. Identification of emotions in music by persons with Parkinson's disease (PD). Box plot of the scores on the four subtests of the emotion recognition task in PD patients (black lines, gray boxes) and controls (gray lines, white boxes). On the happiness subtest all subjects obtained the maximum score, except two subjects (+). For the fear recognition subtask, none of the controls scored below 5, therefore the downward error bar is absent. (Reproduced from van Tricht et al., 2010, with permission.)

Huntington's disease

Woodie Guthrie (1912–1967) is perhaps the most famous musician to have developed Huntington's disease. Guthrie performed during the early stages of the disease, but it eventually affected his music career and ability to sing and play (Arevalo et al., 2001; Innes and Chudley, 2002). His impact on the genre of folk music resulted in his induction into the Rock and Roll Hall of Fame in 1988. The impact of Huntington's disease on the music abilities of Guthrie was never formally studied, but a few studies have examined the processing of music in persons with Huntington's disease. For example, Beste and colleagues (2011) examined the brain response (using functional MRI) to three types of auditory stimulation (music, tones, and syllables) in persons with either premanifest Huntington's disease or manifest Huntington's disease. The music condition included listening to a piano piece by French composer Charles-Valentin Alkan ("Barcarole"). Compared to controls, the persons with Huntington's disease had increased activation in the cerebellum and medial prefrontal cortex and reduced activity in the left parahippocampal gyrus and right fusiform gyrus when listening to a musical composition. In addition, the authors found that the processing of music was correlated with the severity of the movement disorder. Another study used an auditory stimulation paradigm (sequence of tones) and functional MRI methods to examine the basal ganglia-thalamic brain circuits in persons with either premanifest or manifest Huntington's disease (Saft et al., 2008). The authors found reduced activation of basal ganglia-thalamic circuits in premanifest Huntington's disease, but persons with clinically evident Huntington's disease had hyperactivation of the same structures when listening to a sequence of tones. The authors suggested that this pattern reflected functional reorganization of brain areas in an attempt to maintain auditory function.

The basal ganglia has been an area of interest in investigations of sound processing because of its role in attention-dependent temporal processing (Buhusi and Meck, 2005; Langers and Melcher, 2011). In particular, this region interacts with the supplementary motor area and the cerebellum for the temporal processing of sounds Macar et al., 2006; Ivry and Schlerf, 2008; Coull et al., 2011). Apart from these few studies, there does not appear to be any further systematic studies of music processing in persons with Huntington's disease.

Recognition of emotions in music

The link between music and emotions has been debated for centuries. An interest in how humans perceive the emotional content in music or how an emotional response to music is generated has increased in recent years (Juslin and Sloboda, 2010). There are a number of cues that convey emotions in music. For example, a listener may visually perceive the gestures of a performer that reflect emotions. Listeners might also hear musical cues, such as tempo or tonality of a piece, that convey emotional information. For the purposes of this chapter, we will focus on the recognition of emotions while listening to music in persons with dementia.

Several recent studies have examined the recognition of emotions in music in persons with both AD and non-AD dementias. Hsieh and colleagues (2011) studied the recognition of emotions in music with 11 persons with semantic dementia, 12 with AD, and 20 healthy controls. They administered 40 unfamiliar music excerpts that represented four emotions (happy, peaceful, sad, or scary). The participants were asked to listen to the excerpt and select the emotion that best represented the music. Both semantic dementia and AD patients scored lower than controls in identifying the emotions associated with the music, but the semantic dementia patients performed substantially worse than the AD patients. The authors also found that the semantic dementia patients had particular difficulty when identifying negative (sad or scary) compared to positive emotions (happy or peaceful) in the music. In addition, both AD and semantic dementia patients had more difficulty identifying emotions in music than emotions in faces.

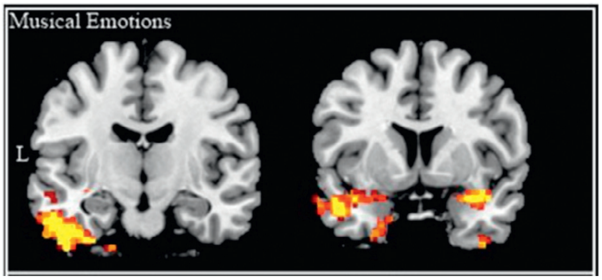

Fig. 37.4. Correlation between performance on music emotions task and brain atrophy. Voxel-based morphometry analyses showing brain regions that correlate with recognition of musical emotions (top left: Montreal Neurological Institute (MNI), $x = -46$, $y = -12$, $z = -46$; top right: MNI, $x = 40$, $y = 6$, $z = -48$). Colored voxels are significant at $P < 0.001$ uncorrected. (Reproduced from Hsieh et al., 2012, with permission.)

A similar pattern was observed in two case studies, one with AD and the other with semantic dementia (Omar et al., 2010). These initial studies suggest that persons with AD and semantic dementia have deficits in recognizing emotions in music when it is just presented as an auditory stimulus.

Hsieh and colleagues (2012) also examined the correlation between the performance on the music emotions task with the amount of atrophy on the brain MRI using voxel-based morphometry. They found that performance on this task was correlated with brain atrophy in the right anterior temporal pole, insula, and amygdala (Fig. 37.4). That is, the patients who had the most difficulty identifying the emotions in the music excerpts had the most atrophy in these areas. Interestingly, there was some overlap between the brain areas involved in perceiving emotions in music and those involved in perceiving emotions in faces. Apart from these few studies with AD and semantic dementia, the recognition of emotions in other types of neurodegenerative disorders is largely unexplored.

PROCESSING OF NON-VERBAL SOUNDS IN NEURODEGENERATIVE DISEASES

In addition to the studies involving music reviewed above, there are a number of other studies that have examined the processing of non-verbal (non-musical) sounds in persons with neurodegenerative diseases. Several authors have provided a framework for categorizing non-verbal sounds that occur in the environment. Taken broadly, there are sounds produced by both living (biologic) and non-living (non-biologic) agents. Within the living category, there are sounds produced by both humans and animals; within the non-living category, there are mechanic and environmental sources of sounds (Griffiths and Warren, 2004; Engel et al., 2009). There have been a number of studies that examine how non-verbal (non-musical) sounds are processed in neurodegenerative diseases.

In one of the early studies about non-verbal sound processing in AD, Rapcsak and colleagues (1989) used a sound–picture-matching task to evaluate the processing of non-verbal sounds in AD. The authors found that patients with mild to severe AD had considerable difficulty selecting the correct picture that corresponded to the non-verbal sound. In contrast, the AD patients had no difficulty selecting the correct picture when the examiner verbalized the names. Other studies have also documented difficulty with selecting pictures to match non-verbal sounds in persons with AD (Eustache et al., 1995; Brandt et al., 2010).

A few studies have examined the processing of environmental sounds in non-AD dementias. For example, Bozeat and colleagues (2000) used 48 sounds from six categories (domestic animals, foreign animals, human sounds, household items, vehicles, and musical instruments) to study non-verbal sound processing in 10 patients with semantic dementia. They asked the patients to match sounds to pictures, sounds to written words, and spoken words to pictures using an array with 10 within-category items. They also administered a neuropsychologic battery of general semantic knowledge. The semantic dementia patients performed below controls on all the tasks involving the environmental sounds. They also found significant correlations between the environmental sounds tasks and verbal tests of semantic knowledge, suggesting that the semantic breakdown in patients with semantic dementia extends to both verbal and non-verbal information.

In another study involving patients with two atypical parkinsonian disorders (corticobasal degeneration, progressive supranuclear palsy), AD, and FTD, Chow and colleagues (2010) examined the naming sounds generated from both manipulable (e.g., hammer) and non-manipulable objects (e.g., train). An item was considered manipulable if the action required to make the sound required manual manipulation by the hand. They found that the patients with corticobasal degeneration or progressive supranuclear palsy named significantly fewer sounds than controls or patients with AD or FTD, who typically do not have prominent motor symptoms. In addition, the corticobasal degeneration and progressive supranuclear palsy patients had a disproportionate impairment in the ability to name the sounds from manipulable objects. Interestingly, action naming and verb production are often impaired in patients with corticobasal degeneration and progressive supranuclear palsy (Bak et al., 2006; Cotelli et al., 2006). These findings suggest that the ability to physically manipulate an object is related to the ability to name an object and suggest a link between the auditory system, cognition, and the motor system. Chow and colleagues (2010) also found a correlation between performance on naming sounds of manipulable objects and gray-matter volume on MRI in the left, premotor areas and left dorsolateral prefrontal cortex.

As discussed above, Goll and colleagues (2012a) recently assessed auditory scene analysis, the ability to parse sound sources in the auditory environment, of both verbal and non-verbal sounds in a cohort of 21 persons with AD. The persons with AD performed much worse than matched controls on both auditory scene analysis tasks, but the performance was somewhat attenuated after accounting for visuospatial working memory. They also found that performance correlated with brain volume in several posterior cortical areas, using voxel-based morphometry of brain MRI. The temporal lobe has also been implicated in the central auditory dysfunction of patients with other neurodegenerative diseases. Patients with semantic dementia showed differential activation of the temporal lobe when listening to animal and tool sounds in a functional MRI paradigm (Goll et al., 2012b) (Figs 37.5 and 37.6). The paradigm involved the perceptual processing of spectrotemporally complex but meaningless sounds and for the semantic processing of environmental sound category (animal sounds versus tool sounds). Thus, anterolateral temporal cortical mechanisms may be necessary for the representation and differentiation of sound categories.

The processing of non-verbal auditory signals has also been studied using electrophysiology and other brain-imaging methods in persons with neurodegenerative diseases. For example, event-related potentials (ERPs) can be measured on the scalp (after stimulus onset) and can provide estimates of the activity of specific brain areas involved in the processing of sensory information. With auditory stimuli, electrical potentials can be measured beginning in the brainstem (as with brainstem auditory evoked potential) up to brain networks involved in both primary and secondary auditory cortices (P50, N100, N200) as well as association cortex (N200, P300). These scalp recordings are often recorded (using electroencephalograph (EEG) electrodes) when participants perform a behavioral task. The oddball task is commonly used in electrophysiologic studies of neurodegenerative diseases. The oddball task requires subjects to listen to a sequence of repeating tones (e.g., 1000 Hz) with a constant speed and press a button when they hear an oddball or deviant tone (e.g., 2000 Hz). In this oddball paradigm, the deviant tones elicit a series of electric potentials that can be measured over time using EEG methods.

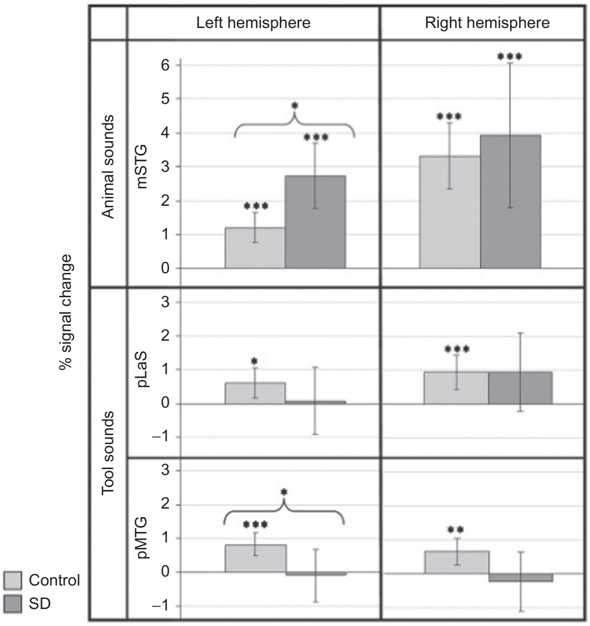

Fig. 37.5. Category-specific contrast effects sampled at previously specified foci of category-specific semantic sound processing. Bars show mean effect sizes (proportionate to percent blood oxygen level-dependent (BOLD) signal change) for the control and semantic dementia (SD) patient groups separately for the category-specific semantic contrast at prespecified foci of category-specific auditory processing (based on Lewis et al., 2005); 95% confidence intervals are also displayed. The upper panels show effects at foci previously associated with animal sound processing in the contrast assessing category-specific semantic processing favoring animal sounds, [(mful_a – mless_a) – (mful_t – mless_t)]; whilst the lower panels show effects at foci previously associated with tool sound processing in the reverse contrast assessing category-specific semantic processing favoring tool sounds, [(mful_t – mless_t) – (mful_a – mless_a)]. Asterisks above bars indicate significance levels for the control and SD groups separately; asterisks above brackets indicate significance levels for between-group comparisons. $*P < 0.05$; $**P < 0.01$; $***P < 0.001$; mSTG, middle superior temporal gyrus; pLaS, posterior lateral sulcus; pMTG, posterior middle temporal gyrus; SD, semantic dementia. (Reproduced from Goll et al., 2012b, with permission.)

Although the various potentials have been studied in persons with dementia, the P300 brain potential is thought to be important in the study of AD, particularly in the early stages. Again, the majority of studies have been done in persons with AD. Persons with AD have long been known to exhibit prolonged peak P300 latency and decreased P300 amplitude (Polich et al., 1990; Holt et al., 1995; Polich and Pitzer, 1999) compared with healthy controls. The differences in amplitude and latency may be used to help differentiate between healthy individuals and those with preclinical or early

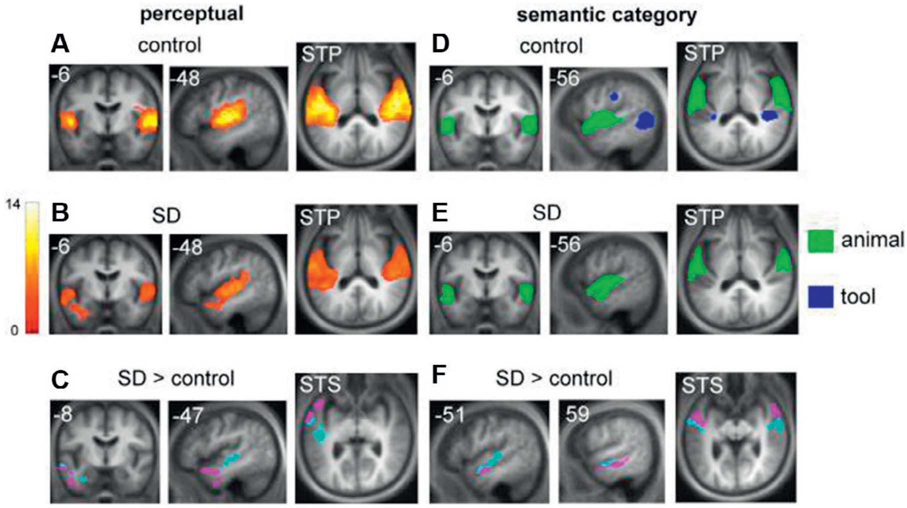

Fig. 37.6. Statistical parametric maps showing activation profiles for perceptual and semantic processing of environmental sounds in healthy controls and patients with semantic dementia. Statistical parametric maps show clusters (formed at whole-brain uncorrected height threshold $P < 0.001$) that are significant at extent threshold $P < 0.05$, family-wise error-corrected for multiple comparisons over the whole brain. Maps are rendered on a composite mean normalized structural brain image; the left hemisphere is shown on the left for all coronal and axial sections. For sagittal and coronal sections the plane is indicated using Montreal Neurological Institute (MNI) coordinates. All axial slices are tilted parallel to the superior temporal plane to show key auditory regions; the anatomic plane of view is indicated. SD, semantic dementia; STP, superior temporal plane; STS, superior temporal sulcus. Panels a and b: the color bar (left) codes voxel-wise T scores for contrast (meaningless sounds > silence). Panel c: all clusters showing a significant interaction with group (patient > control) for the contrast (all meaningless sounds > silence) are depicted in either magenta or cyan. Magenta codes voxels in which controls alone showed greater activation in the reverse contrast (silence > meaningful sounds) than the forwards (meaningless sounds > silence) contrast, indicating that the group interaction within these voxels may be driven by greater activation for controls compared to patients in the reverse contrast. However, remaining voxels, coded in cyan, are likely to be driven by greater activation for patients compared to controls in the forwards contrast. Panels d and e: green codes significant clusters in the contrast assessing the category-specific semantic processing favoring animal sounds, [(mful_a–mless_a) – (mful_t–mless_t)]; blue codes significant clusters in the contrast assessing category-specific semantic processing favoring tool sounds, [(mful_t – mless_t) – (mful_a – mless_a)]. Panel f: all clusters showing a significant interaction with group (patient > control) for the contrast assessing category-specific semantic processing favoring animal sounds are depicted in either magenta or cyan. Magenta codes voxels in which controls alone showed greater activation in the reverse contrast (category-specific semantic processing favoring tool sounds) than the forwards (category-specific semantic processing favoring animal sounds) contrast, indicating that the group interaction within these voxels may be driven by greater activation for controls compared to patients in the reverse contrast; however, remaining voxels, coded in cyan, are likely to be driven by greater activation for patients compared to controls in the forwards contrast. (Reproduced from Goll et al., 2012b, with permission.)

AD (Polich and Pitzer, 1999; Golob et al., 2002, 2007). In another study, Golob and colleagues (2007) found significantly larger P50 and N100 amplitudes (using an auditory oddball task) in amnestic MCI patients who eventually converted to AD, compared with those who remained stable. The P50 and N100 amplitudes were also larger in the MCI converters than those with mild AD, suggesting that these potentials may reflect the neural activity during the transition from MCI to AD. Figure 37.7 shows the P50 and N100 results for each of the groups studied (young adults, older adults, MCI stable, MCI converters, and mild AD). P300 latency was also increased in MCI converters, but the P300 did not differentiate the MCI converters from the mild AD patients.

ERP measures may also be helpful in differentiating dementia etiologies. For example, the P300 latency, amplitude, and topography may differ between individuals with DLB and AD (Bonanni et al., 2010). These measures may also help distinguish between patients with Parkinson's disease with and without cognitive impairment (Nojszewska et al., 2009). Although few in number, ERP methods have also been used to study non-verbal auditory processing and attention in other non-AD dementias, such as Huntington's disease (Uc et al., 2003; Beste et al., 2008), vascular cognitive impairment (Muscoso et al., 2006), and primary progressive aphasia (Onofrjet al., 1994). Thus, auditory potentials may differ according to the degree of cognitive impairment and also help distinguish dementia etiologies.

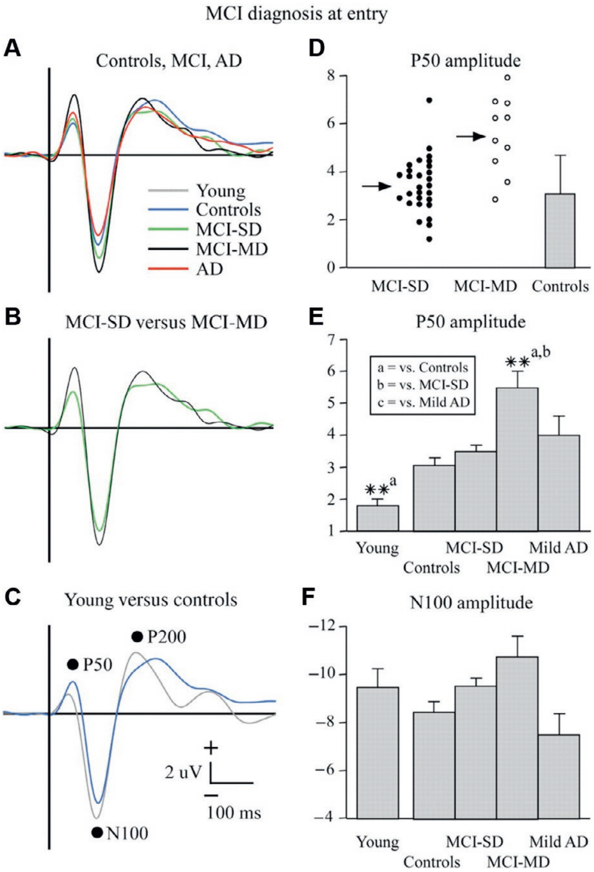

Fig. 37.7. P50 and N100 results for five subject groups. Event-related potentials to non-targets during the baseline session in all older subjects (**A**), mild cognitive impairment (MCI) subtypes (**B**), and young and older controls (**C**). (**D**) P50 amplitudes from individual MCI subjects (MCI single domain (MCI-SD) and MCI multiple domain (MCI-MD)). Mean ± 1 SD from controls are also shown for comparison. Group comparisons of P50 (**E**) and N100 (**F**) amplitudes. Note that in panel F negative potentials are plotted upwards because the N100 is negative in polarity. Vertical lines indicate stimulus onset. Asterisks show *post hoc* tests indicating significant differences between pairs of groups, shown by insert (*$P < 0.05$, **$P < 0.01$). (Reprinted from Golob et al., 2007, with permission.)

MUSIC AS THERAPY FOR DEMENTIA

Music has also been used as a therapeutic intervention for persons with dementia. The music activities range from informal (e.g., background music in assisted-living environments) to more formal approaches, such as with music therapy – defined as the use of music to accomplish specific therapeutic goals within a therapeutic relationship with a board-certified music therapist. Additional information about the use of music with dementia can be found in Clair and Memmott (2008).

The early evidence for the positive impact of music on persons with dementia came out of the music therapy and nursing literature in the 1980s. These studies focused on using music activities to manage behavioral symptoms and increase alertness in persons who were in the severe stages of dementia (Norberg et al., 1986; Millard and Smith, 1989). Since these early studies, the number of studies examining the effect of music interventions on persons with dementia has increased steadily. However, it is important to keep in mind that there are concerns about the methodologic quality of many of these studies, as articulated in the most recent Cochrane Collaboration review (Vink et al., 2004), which was updated in 2011 again with the statement, "There is no substantial evidence to support nor discourage the use of music therapy in the care of older people with dementia" (Vink et al., 2011). The studies have been criticized with regard to the research design, small sample sizes, short length of interventions, and presentation of results. Keeping these limitations in mind, however, the section below will review the primary areas of research and promising leads about the effects of music interventions for persons with dementia. There is clearly a need for higher-quality studies about the therapeutic effects of music on persons with dementia, particularly because non-pharmacologic interventions, like music, can be relatively low-cost to implement and easily translated in many different settings. There is also a need to improve the tools for assessing the effect of music on persons with dementia. This area of inquiry remains of high interest, which can be inferred by the publication of several recent reviews (Wall and Duffy, 2010; McDermott et al., 2012; Raglio et al., 2012).

The majority of research about the therapeutic effects of music for persons with dementia has focused on using music to help reduce behavioral and psychologic symptoms, such as agitation, aggression, anxiety, and depression. A number of studies have concluded that music interventions, such as music listening or group music therapy sessions, were associated with reduced agitation in persons with dementia (Groene, 1993; Clark et al., 1998; Gerdner, 2000; Sung et al., 2006; Janata, 2012). It is important to note that the majority of these studies enrolled persons who met criteria for dementia, but most studies did not stipulate specific dementia diagnoses. It is likely that the effect of music on behavioral symptoms will differ depending on the dementia diagnosis. In a recent study with an improved study design, Vink and colleagues (2012) randomly assigned 77 persons with dementia (34% AD, 21% vascular dementia, 35% other or missing) to either 4 months of music therapy (twice weekly) or recreational activities (active control). Both interventions were associated with a reduction in agitation from before to after the sessions (as measured by a modified version of the Cohen-Mansfield Agitation Inventory), but there were no significant differences between the effects of music or recreational activities on agitation.

Several studies have also found a reduction in symptoms of anxiety and depression after various music interventions. For example, Guetin and colleagues (2009) randomly assigned 30 mild to moderately severe patients with AD in assisted living to either 4 months of weekly music therapy sessions or a control group. The patients with AD who completed the music therapy sessions had significantly lower scores on Hamilton Anxiety Scale scores. This effect persisted another 2 months after the music therapy sessions ended. Other studies also report a reduction in anxiety and depression after various music interventions (Ashida, 2000; Han et al., 2010; Sung et al., 2010, 2012).

Several studies have also attempted to examine the possible effect of music interventions on cognitive function in persons with dementia. For example, one study found improved spontaneous speech content and language fluency (as measured by the Western Aphasia Battery speech subscale) in a group of mild to severely impaired persons with dementia following 2 months of music therapy, compared to conversation sessions. Another study examined the effect of a 12-week Sound Training for Attention and Memory and Dementia (STAM-Dem) program on persons with mild to severe dementia compared to a usual-care group (Ceccato et al., 2012). The authors found that the group with STAM-Dem training had significantly better pre–posttest scores on attention and prose memory but not the test of global cognition (Mini-Mental State Examination). Other studies also document a lack of improvement on the Mini-Mental State Examination after various music interventions (Groene, 1993; Raglio et al., 2008; Guetin et al., 2009). This is not surprising because it is unlikely that global tests of cognition are sensitive enough to detect possible effects of music on cognition. It is difficult to know at this stage whether or not music interventions are an effective tool for managing behavioral symptoms of dementia, in particular, AD. Despite the limitations of the studies, there appear to be promising trends that suggest that music may be an effective therapeutic tool, and additional studies are needed.

Music-based movement therapy (Thaut et al., 1996) has also been used to help improve gait and balance in persons with Parkinson's disease. This type of intervention is based on the premise that the temporal structure in music helps provide meaningful auditory cues that facilitate synchronization of movement, such as gait (Madison et al., 2011). A recent meta-analysis of six randomized controlled trials involving persons with Parkinson's disease concluded that music-based movement therapy had positive effects on several motor outcomes (i.e., Berg Balance Scale, Timed Up and Go, and stride length) but not the Unified Parkinson's Disease rating motor scale (de Dreu et al., 2012). These results suggest that additional research is needed to explore the possible benefit of music-based movement therapy for persons with Parkinson's disease.

SUMMARY

This chapter provided a broad overview of hearing in persons with neurodegenerative diseases, with a particular focus on the auditory processing of music as one type of auditory stimulus. The literature suggests that the processing of music information differs by dementia etiology. Impairments in the central auditory system are common in persons with various neurodegenerative diseases. A number of case reports document a relative preservation of music abilities in persons with AD, particularly for playing a musical instrument, processing of basic aspects of music, and making judgments about familiar melodies. However, persons with AD have difficulty with the short-term memory for music excerpts. Studies with persons with semantic dementia suggest that aspects of music knowledge may remain preserved, although they may have difficulty processing familiar melodies. These studies are few and most include only musically trained individuals. Music-based movement therapy may improve some motor function for persons with Parkinson's disease, while it appears that they have difficulty with rhythm perception or recognizing some emotions in music. The processing of auditory stimuli in persons with Huntington's disease appears to engage brain circuits involved in movement. The evidence for the positive effect of music on managing behavioral symptoms in AD is encouraging, but higher-quality studies are needed. It is important to keep in mind that performance on various music tasks can be affected by the type and severity of dementia. This often makes comparisons across studies difficult. Performance on music tasks can also be affected by the amount of prior music training. The majority of case studies focus on persons who are either professional or amateur musicians, while many of the group studies include persons with different levels of music background. The studies about music processing in neurodegenerative diseases are also helping improve the understanding about how the brain processes music information.

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