CHAPTER 17

Disorders of musical cognition

Lauren Stewart, Katharina von Kriegstein, Simone Dalla Bella, Jason D. Warren and Timothy D. Griffiths

Introduction

The study of the neural underpinnings of musical perception and cognition has advanced greatly since Critchley and Henson published their edited volume *Music and the brain* (1977). Technical advances in functional neuroimaging and the development of theoretical models of musical processing (Peretz and Coltheart 2003) have allowed us to gain an understanding how musical processing occurs in the normal human brain. In parallel with this, the development of musical assessment tools such as the Montreal Battery for the Evaluation of Amusia (MBEA) (Peretz 2003) and the use of MRI to precisely define where lesions occur, allow us to determine which parts of these normal networks are critical for individual aspects of musical processing.

Here we present a comprehensive overview of case studies of acquired disorders of musical listening. The precise details of many of these published case studies are given in a previous review of disordered musical listening (Stewart *et al.* 2006). The current chapter draws general principles from those case studies, as well as presenting and commenting on a number of additional cases of disordered musical production.

Acquired deficits in musical listening

The identification of cases of acquired disorders of musical listening based on symptom profiles in individual patients constitutes the traditional 'symptom-led' approach. An alternative approach to the clinical study of musical deficits has been advocated, based on the study of cases selected on the basis of a particular brain lesion, rather than clinical symptoms: the 'lesion-led' approach. Tables 17.1 and 17.2 refer to symptom-led and lesion-led reports respectively. In the discussion that follows, lesion-led cases will be considered as an adjunct to our primary focus on symptomatic disorders of musical listening.

Examination of the individual cases listed in Table 17.1 demonstrates that a deficit in musical listening can arise as a consequence of a central disturbance of auditory processing: of all the musical listening deficits documented, none could be attributed to a peripheral hearing deficit. As Figure 17.1 shows, the brain lesions that produce deficits in musical listening are widely distributed, with a preponderance of locations in the right hemisphere. However, even though right-sided lesions are more commonly associated with deficits in pitch and other domains, left sided lesions can also produce deficits in these aspects of musical listening. The preponderance of right hemispheric lesions associated with musical listening deficits may, at least partially, reflect a sampling bias: individuals with left hemisphere damage are often aphasic and testing of non-linguistic skills is often difficult and rarely a priority. The majority of cases are attributable to cerebrovascular events, though other pathologies such as focal cerebral degeneration ('progressive amusia') are represented

Table 17.1 Acquired symptom-led reports

Brust 1980 (case 2) (1980)	Mendez and Geehan (MS) (1988)
Confavreux *et al*. (1992)	Murayama *et al*. (2004)
Di Pietro *et al*. (2004)	Patel *et al*. (CN) (1998)
Eustache *et al*. (cases 1, 2) (1990)	Patel *et al*. (IR) (1998)
Fries and Swihart (1990)	Peretz *et al*. (CN) (1994)
Fujii *et al*. (1990)	Peretz *et al*. (CN) (1996)
Griffiths *et al*. (1997)	Peretz *et al*. (IR) (1997)
Griffiths *et al*. (2004)	Peretz *et al*. (IR) (1998)
Griffiths *et al*. (2006)	Peretz and Gagnon (IR) (1999)
Habib *et al*. (1995)	Peretz *et al*. (IR) (2001)
Hattiangadi *et al*. (2005)	Piccirilli *et al*. (2000)
Hofman *et al*. (1993)	Satoh *et al*. (2005)
Johannes *et al*. (1998)	Schon *et al*. (2004)
Johkura *et al*. (1998)	Spreen *et al*. (1965)
Kohlmetz *et al*. (2003)	Tramo *et al*. (MS) (1990)
Lechevalier *et al*. (1984)	Tanaka *et al*. (1987)
Levin and Rose (1979)	Terao *et al*. (2005)
Mavlov (1980)	Tramo *et al*. (MS) (2002)
Mazzoni *et al*. (1993)	Uvstedt (case 9) (1937)
Mazzucchi *et al*. (1982)	Wilson *et al*. (2002)

(Confavreux *et al*. 1992). Because of the nature of these lesions, musical listening disorders are rarely 'pure': over half the cases are associated with disorders of speech perception, and approximately a third of cases with disorders of environmental sound perception. In most cases available data on speech processing are limited, preventing clear comment about the general association of directly related speech deficits (e.g., perceptual dysprosody) or other deficits in the speech domain. There is some evidence to suggest that the earlier stages of an acquired deficit in musical listening (e.g. less than one year after onset) tend to be accompanied by more deficits in listening to other classes of sounds suggesting a disorder in musical listening that can emerge as an isolated deficit following the recovery phase of a more generalized auditory agnosia.

Figure 17.1 shows that many areas are implicated in more than one function. However, it is clear that the necessary bases for music processing are separable: within the domain of music, relatively isolated deficits of pitch (Peretz *et al*. 1994), temporal (Mavlov 1980), timbral (Kohlmetz *et al*. 2003), mnemonic (Peretz 1996) and emotional (Griffiths *et al*. 2004) processing have all described. More fine-grained dissociations also occur: for instance, between pitch interval and pitch contour (Liegeois-Chauvel *et al*. 1998; Peretz 1990) and between rhythm and metre (Di Pietro *et al*. 2004; Wilson *et al*. 2002).

Pitch: interval

Deficits in the analysis of pitch intervals (the detection of a pitch change and/or the discrimination of the direction of a pitch change) are most strongly associated with lesions involving lateral Heschl's Gyrus (HG) and non-primary auditory cortical areas in Planum Temporale (PT) and the parieto-temporal junction (Figure 17.1). The detection of pitch differences and the discrimination of pitch direction are functionally

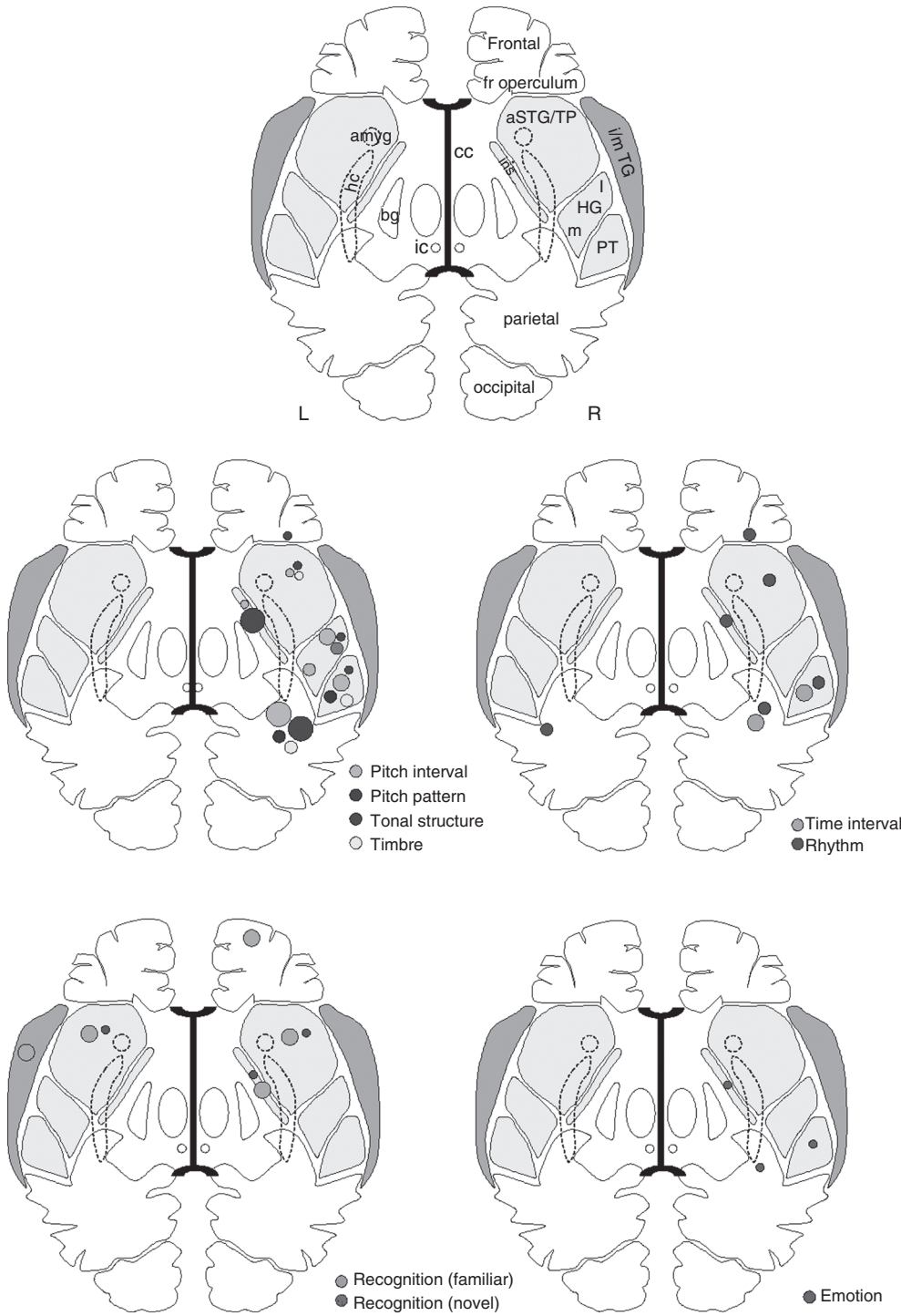

Fig. 17.1 Critical brain substrates for musical listening disorders. This data is based on the symptomatic cases of musical listening disorder (Table 17.1). The detailed analysis of these cases is

separable, but have been distinguished only infrequently in symptom-led studies. Where it has been specifically assessed, impaired pitch-difference detection is generally associated with involvement of subcortical structures and ascending auditory pathways or primary auditory cortex in medial HG (Habib *et al.* 1995, Hattiangadi *et al.* 2005, Terao *et al.* 2006, Tramo *et al.* 2002) while impaired pitch-direction discrimination is generally associated with involvement of lateral HG (Lechevalier *et al.* 1984, Tanaka *et al.* 1987, Terao *et al.* 2005, Tramo *et al.* 2002).

These data are congruent with evidence from temporal lobectomy series (Table 17.2). Right-lateral HG resection leads to deficits in the detection of pitch-change direction in pure tones (Johnsrude *et al.* 2000) and complex tones (Zatorre 1988) These findings, especially the latter, suggest that aspects of pitch perception, as opposed to the sensory representation of frequency- and time- domain properties of the stimulus, depend on the integrity of cortical areas beyond primary auditory cortex.

Pitch: pattern

Deficits in the analysis of pitch patterns, such as melodies, are common in acquired disorders of musical listening (Table 17.1). The deficits are most often associated with lesions posterior to HG, in PT and the parieto-temporal junction, and anterior to HG in anterior superior temporal gyrus (STG) (Figure 17.1). These lesions are more common on the right. Melody discrimination has also been widely assessed in the lesion-led literature (Table 17.2): right but not left temporal lobectomy impairs discrimination of pitch pattern, even where HG is not included (Milner 1962). However, inclusion of HG produces deficits in melody perception over and above those due to the resection of the temporal lobe anterior to it (Samson and Zatorre 1988, Zatorre 1985). In a study comparing resections involving posterior versus anterior STG (Liegeois-Chauvel *et al.* 1998), posterior resection was associated with more severe impairment of pitch pattern perception; this effect could not be attributed to involvement of HG. Right anterior temporal lobe resections have also been associated with impaired working memory for pitch (Zatorre and Samson 1991) which is likely to affect perception of long-term structure in melodies, and more specifically, discrimination tasks requiring comparisons between sequential stimuli.

Pitch contour (the pattern of 'ups' and 'downs' in a melody) and the associated absolute pitch values can be considered as corresponding to psychologically distinct 'global' and 'local' levels of pitch processing, respectively (Dowling and Harwood 1985). These levels can be probed by tasks which require discrimination of melodies with different pitch contour ('global' tasks) or different absolute pitch values with the same contour ('local' tasks), respectively. A 'pure' global task would require transposition

presented in supplementary Table 1 of Stewart *et al*. (2006). Five cartoons are shown, each depicting the brain in a schematic axial section that includes all key anatomical areas involved in music listening (identified on the top cartoon); the corpus callosum (black), superior temporal plane (light grey) and middle/inferior temporal gyri (dark grey areas, in exploded view) are coloured for ease of identification. Musical functions 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 Stewart *et al*. (2006) have been thresholded; the presence of a coloured circle corresponding to a particular function in a region indicates that at least 50 per cent 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. Metre is not represented as no brain area was implicated in 50 per cent or more of cases. amyg, amygdala; aSTG, anterior superior temporal gyrus; bg, basal ganglia; cc, corpus callosum; fr, frontal; hc hippocampus; HG, Heschl's gyrus; i, inferior; ic, inferior colliculi; ins, insula; l, lateral; m, medial; PT, planum temporale; TG, temporal gyrus. See colour plate section. This figure is taken from Stewart L, Von Kriegstein K, Warren JD and Griffiths TD. Disorders of musical listening. *Brain* 2006, 129, 2533–2553, by permission of Oxford University Press.

Table 17.2 Acquired lesion-led reports

Resection cases	Stroke/other type of lesion
Gosselin *et al*. (2005)	Alcock *et al*. (2000)
Johnsrude *et al*. (2000)	Ayotte *et al*. (2000)
Kester *et al*. (1991)	Grossman *et al*. (1981)
Liegeois-Chauvel *et al*. (1998)	Kinsella *et al*. (1988)
Milner (1962)	Peretz (1990)
Samson and Zatorre (1988)	Prior *et al*. (1990)
Samson and Zatorre (1991)	Robin *et al*. (1990)
Samson and Zatorre (1992)	Samson *et al*. (2001)
Samson and Zatorre (1994)	Schuppert *et al*. (2000)
Samson *et al*. (2001)	Shapiro *et al*. (1981)
Samson *et al*. (2002)	Sidtis and Volpe (1988)
Shankweiler (1966)	Tramo and Bharucha (1991)
Warrier and Zatorre (2004)	
Zatorre (1985)	
Zatorre (1988)	
Zatorre and Halpern (1993)	
Zatorre and Samson (1991)	

between the melodies compared (like a shift in key) to prevent the use of any local information. However, this renders the task much harder for non-musicians and the MBEA does not employ it. Peretz (1990) showed that patients with right cerebral hemisphere strokes could process neither global nor local information in melodies, while patients with strokes involving the left hemisphere could process global but not local information. Isolated impairments of local processing were observed, but isolated impairments of global processing were not, leading Peretz to propose an influential hierarchical model of co-operation between the hemispheres. According to this model, the right hemisphere derives pitch contour which is then elaborated upon by the left hemisphere which fills in the detailed pitch structure. In the model, prior contour processing is necessary for absolute pitch values to be processed: lesions involving the right hemisphere therefore compromize the processing of both contour and the absolute values of pitch whereas lesions involving the left hemisphere prevent absolute pitch values being added to the contour provided by the right hemisphere. This model was supported by the findings of a temporal lobectomy series (Liegeois-Chauvel *et al.* 1998). However, other neuropsychological and functional imaging evidence suggests that hemispheric differences are less clearcut (Schuppert *et al.* 2000, Stewart *et al.* 2008).

Pitch: tonal structure

Tonal structure refers to rule-based patterns of pitch determined by key. While both tonal and atonal pitch patterns exhibit global and local structure, tonal structure is specific to tonal music (i.e., most Western music composed before the twentieth century). The most widely used test of this type of processing is the key violation task in the MBEA, which assesses the ability of subjects to detect notes that are out of key. Deficits in tonal analysis have been associated with damage involving a predominantly right-sided network of non-primary auditory cortical areas including lateral HG, PT, parieto-temporal junction, insula, anterior STG and frontal operculum (Figure 17.1). The frontal opercular involvement is proportionately greater

relative to its involvement in other aspects of pitch processing, but the number of studies is small.

Timbre

Timbral perception has a number of dimensions that can be related to different acoustic properties of the incoming sound, and lesions affecting any or all of these dimensions could in principle lead to a deficit of timbre perception. Many clinical studies include reports of perceptual alterations in the perceived quality of music (often described as unpleasant, 'flat' or 'mechanical' in nature) or inability to recognize musical instruments, which might represent specific deficits of timbre perception. However, timbre as a distinct functional component of music has only been assessed infrequently in the clinical literature. This evidence suggests that a network of areas in the right superior temporal lobe that overlaps closely with areas implicated in pitch-pattern analysis is critical for normal timbre perception (Figure 17.1). Timbral deficits have generally been observed in conjunction with pitch-pattern deficits, however timbral deficits with spared pitch-pattern perception have also been described after strokes involving right STG (Kohlmetz *et al.* 2003, Mazzucchi *et al.* 1982). The deficits may extend to the discrimination of timbre in voices and environmental sounds (Mazzucchi *et al.* 1982).

These findings from the symptom-led literature are mirrored by studies of temporal lobectomy series (Table 17.2). Right temporal lobectomy leads to deficits in the perception of timbral change when this is in the spectral dimension (Milner 1962, Samson and Zatorre 1994), temporal dimension (Samson and Zatorre 1994), or both (Samson *et al.* 2002). This last study also suggested a subtle effect of left temporal lobectomy deficit on the processing of timbre associated with melodies but not single notes.

Temporal structure: time interval, rhythm and metre

Like pitch perception, the perception of timing information in music can be analysed hierarchically: the lowest level of temporal processing that we consider here corresponds to the detection of simple durational differences in a tone or detection of a silent interval between two tones. These basic timing elements can be built into more complex structures embedded in metre and rhythm. Schuppert and colleagues (2000) propose a hierarchal scheme where metre and rhythm can be considered as global and local properties in the time domain. The symptom-led evidence implicates predominantly right-sided non-primary auditory cortical areas posterior to HG in the perception of time-interval differences, and bilateral areas widely distributed beyond HG in the perception of rhythm (Figure 17.1). Evidence from lesion-led studies broadly supports a bilateral organization: impaired durational processing has been described following right temporal lobectomy (Milner 1962) and impaired gap detection following left temporo-parietal strokes (Robin *et al.* 1990). Impaired detection of rhythmic violations has been described in left temporo-parietal stroke (Robin *et al.* 1990) and left hippocampal sclerosis (Samson *et al.* 2001), while other studies have not demonstrated laterality differences (Peretz, 1990, Schuppert *et al.* 2000, Shapiro *et al.* 1981). At least some of these apparent discrepancies in lateralization may reflect task effects: for example, the detection of rhythmic errors in familiar tunes (Prior *et al.* 1990, Samson *et al.* 2001) may require musical processing that is not required for the discrimination of simple rhythmic patterns.

Comparatively few studies of metrical processing have been conducted and evidence for a critical brain substrate remains inconclusive. This is likely to be due at least in part to the difficulty of assessing metre reliably, particularly in subjects without formal musical training. In the small symptom-led literature, impairments of metre perception have been associated with individual lesions widely distributed in both cerebral hemispheres. This pattern has been echoed in lesion-led studies. In temporal lobectomy series, Liegeois-Chauvel *et al.* (1998) found metrical impairments following left and right anterior temporal lobe resections, while Kester *et al.* (1991) found a specific decrement in performance following right but not left anterior temporal resection. Ayotte *et al.* (2000) and Peretz *et al.* (1990) both found that stroke patients with heterogeneous left and right hemisphere strokes

were not impaired relative to neurologically normal control subjects, while Schuppert *et al.* (2000) found that both left and right hemispheric stroke patients were impaired relative to controls.

Memory: familiar and novel material

Impaired recognition of familiar tunes is described in a number of studies (Ayotte *et al.* 2000, Griffiths *et al.* 1997, Johannes *et al.* 1998, Lechevalier *et al.* 1984, Peretz *et al.* 1998, Peretz and Gagnon 1999, Peretz *et al.* 1994, Piccirilli *et al.* 2000, Satoh *et al.* 2005, Wilson *et al.* 2002). In all these cases, recognition problems were accompanied by impaired pitch-pattern perception. However, perception and recognition can sometimes dissociate. Patients may have intact perception but impaired recognition (Eustache *et al.* 1990 (case 1), Peretz 1996) or the converse (Eustache *et al.* 1990 (case 2); Schuppert *et al.* 2000).

Figures 17.1 demonstrates that deficits in the perception and recognition of familiar tunes may occur with damage in either cerebral hemisphere involving the anterior STG and insula (Lechevalier *et al.* 1984, Peretz *et al.* 1998, Peretz and Gagnon 1999, Peretz *et al.* 1994, Satoh *et al.* 2005). In the lesion-led literature, familiar-tune recognition was found to be deficient specifically in association with damage involving the right insula (Ayotte *et al.* 2000).

Impaired recognition of novel material is tested in the incidental memory test from the MBEA, which assesses implicit encoding and retrieval of novel musical material. Clinical impairments of musical incidental memory are associated with damage involving a bilateral network of areas that closely overlaps the network implicated in the recognition of familiar tunes (Figure 17.1), and extends into left middle and inferior temporal cortex. In temporal lobectomy series, incidental memory deficits have been described following both right and left anterior resections (Samson and Zatorre 1992, Zatorre 1985).

Emotion

Most people listen to music purely for the aesthetic pleasure it brings. A loss of enjoyment in musical listening is a common presenting complaint in clinical disorders of musical listening. In many cases, this loss of pleasure is accompanied by a perceptual derangement: 'like an out of tune child's dulcimer', (Griffiths *et al.* 1997), 'mechanical' (Griffiths *et al.* 2006), or 'instruments [may lose] their distinctive features of timbre and sound dull' (Piccirilli *et al.* 2000). Associated impairments of pitch-pattern perception (Habib *et al.* 1995) and generalized auditory agnosia (Mazzucchi *et al.* 1982) have been documented. The most consistent association of altered emotional response to music across studies is damage involving the right posterior temporal lobe and insula (Figure 17.1). However, few clinical studies have specifically assessed musical emotion.

Just as perception and recognition for musical material may dissociate, so too may perception and emotional response to music. Isolated deficits of musical emotional response have been described: the patient of Griffiths *et al.* (2004) had been used to experiencing an emotional transformation while listening to Rachmaninov preludes (the 'shiver down the spine' phenomenon) but this was lost following an infarction involving left amygdala and insula. In a temporal lobectomy series (Gosselin *et al.* 2005), patients who had undergone resections of the left or right medial temporal lobe, including the amygdala but sparing the STG, found fearful music less scary than a group of matched controls. Conversely, intact emotional response despite impaired music perception has also been observed (Lechevalier *et al.* 1984, Peretz *et al.* 1998, Peretz and Gagnon 1999). The patient of Peretz *et al.* (1998) still derived pleasure from music, and was able to classify tunes as happy or sad and to discriminate tunes based on emotional tone despite severe perceptual and recognition impairments.

Developmental deficits in musical listening

Case reports of lifelong tone deafness go back more than a century (Grant-Allen 1898), but it has only been in the last five years that the condition has undergone systematic investigation using the same tools that have been applied to

acquired disorders of musical listening. The disorder was first characterized in this way by Peretz and colleagues using the MBEA and given the label 'congenital amusia' (Ayotte *et al.* 2002). This is not the same as what is commonly known as 'tone-deafness', a term which many people apply to themselves, mostly based on the belief that they cannot sing in tune (Sloboda *et al.* 2005, Cuddy *et al.* 2005). Infact, given normal brain development and opportunities for informal singing, the majority of the population can sing in tune (but see Bradshaw and McHenry 2005, Dalla Bella *et al.* 2007 for evidence that singing output may be impaired despite normal perception). Those with congenital amusia, on the other hand, cannot sing in tune, but this is likely to be a consequence of them having a true perceptual agnosia, in which the perception of music is abnormal in the presence of normal hearing and otherwise preserved cognition.

Pitch

Formal characterization of musical perception using the MBEA (Ayotte *et al.* 2002) demonstrates consistent deficits in the domain of pitch-pattern perception (pitch contour, absolute pitch value and key structure). Foxton *et al.* (2004) carried out tests in which types of pitch pattern that are more basic than melody are assessed. The group of subjects identified as having amusia using the MBEA were found to have abnormal perception of pitch change and pitch direction, the most striking changes being demonstrated for pitch direction. Most subjects in the amusic group had thresholds for the identification of pitch direction that were well above a semitone and likely relevant to the perception of Western music. This finding has been recently replicated in an independent group of amusic individuals (Griffiths *et al.* 2007). Given that pitch direction can be thought of as a 'building block' for contour (the pattern of 'ups' and 'downs' in a melody), this work suggests a fundamental deficit in pitch processing that is below the level of melody processing. However, the presence of such a causative deficit would predict that the deficit could be overcome by creating melodic sequences with large intervals. The fact that this is not the case (Foxton *et al.* 2004) argues against a simple low-level deficit in pitch direction as a single causal mechanism for melodic deficits in amusia. However, it remains possible that an inability to analyse pitch direction leads to a failure to develop normal pitch-pattern perception.

Temporal structure

Subjects who have been recruited on the basis of lifelong musical difficulty and score below threshold on the pitch subtests of the MBEA may also have problems with 'following the beat' and with dancing, consistent with a deficit in the analysis of metre and rhythm. Hyde and Peretz (2003) found that although subjects with congenital amusia had a deficit in detection of pitch changes in an otherwise monotonic sequence, their detection of a change in the timing of a note in an otherwise regular sequence was normal. A subsequent study in a different group of amusics (Foxton *et al.* 2006) replicated the finding of normal detection of timing deviation within simple rhythms, but showed that when subjects were required to detect the same deviation in a melodic, as opposed to monotonic context, their performance was impaired. The results support a model in which the abnormal perception of pitch pattern in amusia also affects the perception of the temporal structure of music. It is also worth noting that the amusic individuals so far studied have been recruited using adverts that conceptualize musical difficulties in terms of tune rather than time. In contrast, a large number of individuals screened using an internet version of the scale and rhythm subtest of the MBEA (www.delosis.com/listening/home.html) suggest that certain individuals have specific difficulties with time, but not tune (unpublished observations). This is a potentially novel subtype of amusia with a distinct cognitive and neural basis.

Emotion

A recent questionnaire-based study (McDonald and Stewart 2008) shows that, as a group, those with developmental amusia do not implement music in their everyday lives in the same way as age, gender and training matched controls. They regard the presence of music in public places more negatively than controls and report

significantly fewer emotional responses to music. However, there is considerable individual variation with respect to this. For instance, some amusics report enjoyment of music while others find it unpleasant. The dissociation between the perception of music and its self-reported emotional effects is consistent with evidence from normal functional imaging and clinical studies of acquired lesions that suggest distinct substrates for perception and appreciation but the reasons for such variability are presently unknown.

Neural substrate

The brain basis for congenital amusia has not been extensively investigated. These individuals do not have a history of neurological damage, and structural brain imaging using MRI reveals no gross structural differences. The technique of voxel-based morphometry allows structural MRI data from two or more groups of individuals (e.g. amusic versus non-amusic individuals) to be interrogated with regard to potential regional differences in grey and white matter density. Recent studies have demonstrated structural differences in the inferior frontal lobe and temporal cortex (Hyde *et al*. 2005, 2007; Mandell *et al*. 2007) and EEG studies of responses to pitch changes have demonstrated normal N1 responses to tones but abnormal N2-P3 responses at longer latency (Peretz *et al*. 2005). The N1 response arises from the PT whilst the longer latency responses have a number of more distributed generators. Congruent with the work based on structural MRI, this work suggests brain abnormalities in amusia that may occur in areas quite distinct from auditory cortex. Further studies will be required to ascertain the locus and nature of the abnormality in these developmental cases.

Acquired disorders of musical production

Music production deficits such as impaired singing (vocal amusia or oral-expressive amusia), or deficient music performance on an instrument (expressive instrumental amusia or musical apraxia) have been generally referred to as 'expressive amusia' (Benton 1977). Although cases of musical production deficits have been described since the nineteenth century (reviewed in Benton 1977), there is a paucity of studies of instrumental amusia (Botez and Wertheim 1959; McFarland and Fortin 1982). For this reason, the following discussion will focus on acquired deficits in singing.

Impaired vocal performance (e.g., poor singing of well-known songs) consequent to brain damage has been documented in skilled professional singers and in nonmusicians (for reviews, see Ackermann *et al*. 2007; Gordon *et al*. 2006; Marin and Perry 1999). Early case reports indicate that lesions of the right-hemisphere frontoinsular cortex disrupt the ability to sing, hum or whistle a tune (Mann 1898, 1933; Jossmann 1926, 1927, cited in Benton 1977; Botez and Wertheim 1959). For example, Mann (1898 cited in Benton 1977) reported impaired abilities to sing and whistle songs in a professional singer following injury of the right frontal lobe. Despite the dramatic vocal expression disorder, the patient was still able to recognize familiar songs and did not show any signs of aphasia. Similar cases of musicians exhibiting poor singing in absence of language disorders and with relatively spared music perception and recognition were reported by Jossmann (1926, 1927) and Botez and Wertheim (1959). These findings are consistent with the observation that unilateral inactivation of the right hemisphere (i.e., with the Wada test, see Gordon and Bogen 1974) alter the ability to sing, hum or whistle a tune. Unfortunately, however, most of these case descriptions are anecdotal, thus lacking systematic assessment of music production and perception abilities.

More systematic studies of singing deficits (both symptom-led and lesion-led) are included in Tables 17.1 and 17.2. Confavreux *et al*. (1992) report on a patient who suffered focal cerebral degeneration of right-hemisphere regions involving the anterior temporal gyrus and the insula. Music perception abilities were relatively preserved in the presence of impaired singing and expressive aprosody in speech. More recently, Schön and collaborators (2004) presented the case of IP, a tenor singer with right hemisphere lesions distributed in the inferior frontal gyrus, posterior temporal lobe and inferior parietal lobe. IP is a pure case of vocal amusia exhibiting a specific deficit of in the production of musical intervals. In contrast, production of

rhythm and contour were spared, as was musical perception and language abilities. In order to examine the role of the right and left hemispheres in pitch and rhythm vocal production, Alcock *et al.* (2000) examined vocal performance and music perception in a group study of patients with unilateral left- or right-hemisphere lesions. They found that left-hemisphere patients were mostly impaired in perceiving and reproducing rhythms, without difficulties in singing the correct pitch. Right-hemisphere patients, in contrast, had great difficulties in pitch production and perception tasks, with less marked rhythm processing disorders than left-hemisphere patients. Additional evidence confirming that the right hemisphere is engaged in pitch production comes from two recent single case studies in which acoustical measures of singing proficiency were obtained (Murayama *et al.* 2004; Terao *et al.* 2006). In sum, evidence from symptomatic case studies and lesion-led reports, in general, confirm what has been described in early reports, that the right hemisphere (mostly the frontal-insular regions) is central to vocal musical pitch production. In addition, vocal performance disorders can occur in a pure form in absence of perceptual and linguistic deficits, and may concern very specific aspects of music vocal production (e.g., interval production) while leaving other functions intact.

Further evidence indicating a predominant right-hemisphere involvement in vocal pitch performance comes from neuroimaging and TMS studies. In an fMRI study, Riecker *et al.* (2000) found that speech and singing without lyrics engage opposite hemispheres (at the level of anterior insula), with a left-hemisphere dominance for speaking and a right-hemisphere dominance for singing. A similar lateralization pattern was yielded by a PET study in which speaking and singing with words were contrasted (Jeffries *et al.* 2003). In addition, when TMS was applied over left-hemisphere regions traditionally related to speech production (e.g., near Broca's area) speech was disrupted; similar stimulation over homologous brain areas in the right hemisphere impaired singing, at least for some of the participants (Epstein *et al.* 1999; Lo and Fook-Chong 2004; Stewart *et al.* 2001).

A classical interpretation of these findings is that singing familiar songs engages right-hemisphere regions in contrast to propositional speech which engages the left-hemisphere. This account has gained credence from clinical reports that patients suffering from motor aphasia are still able to sing previously learned songs with well-articulated and linguistically intelligible words (e.g., Assal *et al.* 1977; Yamadori *et al.* 1977). However, the evidence is not clear-cut. Poor singing often emerges in association with linguistic deficits resulting from left-hemisphere damage (e.g. Benton 1977). Furthermore, bilateral hemispheric involvement in sung performance is substantiated by evidence that lesions in either of the two hemispheres impair sung performance (Kinsella *et al.* 1988; Prior *et al.* 1990), that both right- and left-hemisphere anesthetization interfere with singing (Borchgrevink 1980; Zatorre 1984), and that singing without words do no elicit any lip-opening asymmetry, as a measure of laterality (e.g., Cadalbert *et al.* 1994; Hough *et al.* 1994). Finally, clinical observations that motor aphasics can articulate words better when singing than when speaking were not fully corroborated by recent systematic studies (Hébert *et al.* 2003; Racette *et al.* 2006). In sum, it is likely that singing is characterized by less strict lateralization than is speech.

Conclusion

Like any cognitive faculty, music is multifaceted and the identification of the neural basis of any complex faculty must proceed, hand in hand, with an elucidation of its cognitive architecture. The past decade has seen an evolution in the theoretical models of musical processing, allowing the development of theoretically motivated instruments for the systematic evaluation of musical disorders. Such developments have allowed reports of musical disorders to evolve from historical anecdotes to systematic, verifiable accounts which can play a critical role in contributing to our understanding of the cognitive neuroscience of music.

Acknowledgements

L.S, T.D.G and J.W were supported by the Wellcome Trust. L.S. was additionally supported by the Economic and Social Research Council and J.W. received support from a EC grant to the APOPIS consortium. SDB received an integration grant from the European Commission.

References

Ackermann H, Wildgruber D and Riecker A (2006). Singing in the (b)rain: cerebral correlates. In E Altenmüller, M Wiesendanger, J Kesselring, eds, *Music, motor control and the brain*, 205–222. Oxford University Press, Oxford.

Alcock KJ, Wade D, Anslow P and Passingham RE (2000). Pitch and timing abilities in adult left-hemisphere dysphasic and right-hemisphere damaged subjects. *Brain and Language*, **75**(1), 47–65.

Assal G, Buttet J and Javet RC (1997). Musical aptitude in aphasics. *Revue Medicale de la Suisse Romande*, **97**(1), 5–12.

Ayotte J, Peretz I and Hyde K (2002). Congenital Amusia. A group study of adults afflicted with a music-specific disorder. *Brain*, **125**, 238–251.

Ayotte J, Peretz I, Rousseau I, Bard C, Bojanowski M (2000). Patterns of music agnosia associated with middle cerebral artery infarcts. *Brain*, **123**, 1926–1938.

Benton AL (1977) The amusias. In M Critchley and RA Henson, eds, *Music and the brain*, 378–397. William Heinemann, London.

Botez MI and Wertheim N (1959) Expressive aphasia and amusia following right frontal lesion in a right-handed man. *Brain*, **82**, 186–202.

Borchgrevink HM (1980) Cerebral lateralization of speech and singing after intracarotid amytal injection. In MT Sarno and O Hook, eds, *Aphasia. Assessment and Treatment*, 186–191. Stockholm: Almqvist and Wiksell

Bradshaw E and McHenry MA (2005) Pitch discrimination and pitch-matching abilities of adults who sing inaccurately. *Journal of Voice*, **14**(3), 431–439.

Brust JC (1980) Music and language: musical alexia and agraphia. *Brain*, **103**, 367–392.

Cadalbert A, Landis T, Regard M and Graves RE (1994) Singing with and without words: hemispheric asymmetries in motor control. *Journal of Clinical and Experimental Neuropsychology*, **16**(5), 664–670.

Confavreux C, Croisile B, Garassus P, Aimard G and Trillet M (1992). Progressive amusia and aprosody. *Archives of Neurology*, **49**, 971–6.

Critchley M and Henson RA (eds) (1977) *Music and the brain. Studies in the neurology of music.* Heinemann, Oxford.

Cuddy LL, Balkwill L-L, Peretz I and Holden RR (2005). Neuropsychological assessment of musical difficulties: a study of 'tone deafness' among university students. Annals of the New York Academy of Sciences, 1060, 311–324.

Dalla Bella, S, Giguère J-F and Peretz I (2007) Singing proficiency in the general population. *Journal of The Acoustical Society of America*, **121**, 1192–1189.

Di Pietro M, Laganaro M, Leemann B and Schnider A (2004). Receptive amusia: temporal auditory processing deficit in a professional musician following a left temporo-parietal lesion. *Neuropsychologia*, **42**, 868–877.

Dowling WJ and Harwood DL (1985). Music and cognition. Academic Press, London.

Epstein CM, Meador KJ, Loring DW, Wright RJ, Weissmann JD, Sheppard S, Lah JJ, Puhalovich F, Gaitan L and Davey KR (1999) Localization and characterization of speech arrest during transcranial magnetic stimulation. *Clinical Neurophysiology*, **110**(6), 1073–1079.

Eustache F, Lechevalier B, Viader F and Lambert J (1990). Identification and discrimination disorders in auditory perception: a report on two cases. *Neuropsychologia*, **28**, 257–270.

Foxton JM, Dean JL, Gee R, Peretz I and Griffiths TD (2004) Characterization of deficits in pitch perception underlying tone deafness. *Brain*, **127**, 801–110.

Foxton JM, Nandy RK and Griffiths TD (2006). Rhythm deficits in tone deafness. *Brain and Cognition*, **62**(1), 24–29.

Fries W and Swihart AA (1990). Disturbance of rhythm sense following right hemisphere damage. *Neuropsychologia*, **28**, 1317–23.

Fujii T, Fukatsu R, Watabe S, Ohnuma A, Teramura K, Kimura I *et al.* (1990) Auditory sound agnosia without aphasia following a right temporal lobe lesion. *Cortex*, **26**, 263–268.

Gordon HW and Bogen JE (1974) Hemispheric lateralization of singing after intracarotid sodium amylobarbitone. *Journal of Neurology, Neurosurgery, and Psychiatry*, **37**, 727–738.

Gordon RL, Racette A and Schön D (2006) Sensory-motor networks in singing and speaking: a comparative approach. In E Altenmüller, M Wiesendanger and J Kesselring, eds, *Music, motor control and the brain*, 223–238. Oxford University Press, Oxford.

Gosselin N, Peretz I, Noulhiane M, Hasboun D, Beckett C, Baulac M *et al.* (2005) Impaired recognition of scary music following unilateral temporal lobe excision. *Brain*, **128**, 628–40.

Grant-Allen (1878). Note-deafness. *Mind*, **10**, 157–167.

Griffiths TD, McDonald C, Kumar S, Deutsch D, Chinnery P and Stewart L (2007). Could a congenital disorder of musical perception ever be explained by a single gene? International Workshop on the Biology and Genetics of Music, Bologna, Italy.

Griffiths TD, Rees A, Witton C, Cross PM, Shakir RA and Green GG (1997). Spatial and temporal auditory processing deficits following right hemisphere infarction. A psychophysical study. *Brain*, **120**, 785–794.

Griffiths TD, Warren JD and Jennings AR (2006). Dystimbria: a distinct musical syndome? Presented at the International Conference for Musical Perception and Cognition.

Griffiths TD, Warren JD, Dean JL and Howard D (2004). When the feeling's gone: a selective loss of musical emotion. *Journal of Neurology, Neurosurgery and Psychiatry*, **75**, 344–345.

Grossman M, Shapiro BE and Gardner H (1981). Dissociable musical processing strategies after localized brain damage. *Neuropsychologia*, **19**, 425–433.

Habib M, Daquin G, Milandre L, Royere ML, Rey M, Lanteri A *et al.* (1995) Mutism and auditory agnosia due to bilateral insular damage—role of the insula in human communication. *Neuropsychologia*, **33**, 327–339.

Hattiangadi N, Pillion JP, Slomine B, Christensen J, Trovato MK and Speedie LJ (2005). Characteristics of auditory agnosia in a child with severe traumatic brain injury: a case report. *Brain and Language*, **92**, 12–25.

Hébert S, Racette A, Gagnon L and Peretz I (2003). Revisiting the dissociation between singing and speaking in expressive aphasia. *Brain*, **126**(8), 1838–1850.

Hofman S, Klein C and Arlazoroff A (1993). Common hemisphericity of language and music in a musician. A case report. *Journal of Communication Disorders*, **26**, 73–82.

Hough MS, Daniel HJ, Snow MA, O'Brien KF and Hume WG (1994) Gender differences in laterality patterns for speaking and singing. *Neuropsychologia*, **32**, 1067–1078.

Hyde KL and Peretz I (2003) Out-of-pitch but still in-time. An auditory psychophysical study in congenital amusic adults. *Annals of the New York Academy of Sciences*, **999**, 173–176.

Hyde KL, Lerch JP, Zatorre RJ, Griffiths TD, Evans AC and Peretz I (2007). Cortical thickness in congenital amusia: when less is better than more. *Journal of Neuroscience* **27**(47), 13028–13032.

Hyde KL, Zatorre RJ, Griffiths TD, Lerch JP and Peretz I (2005). Morphometry of the amusic brain: a two-site study. *Brain*, **129**, 2562–2570.

Jeffries KJ, Fritz JB and Braun AR (2003) Words in melody: an $H_2{}^{15}O$ PET study of brain activation during singing and speaking. *Neuroreport*, **15**(5), 749–754.

Johannes S, Jobges ME, Dengler R and Munte TF (1998). Cortical auditory disorders: a case of non-verbal disturbances assessed with event-related brain potentials. *Behavioural Neurology*, **11**, 55–73.

Johkura K, Matsumoto S, Hasegawa O and Kuroiwa Y (1998). Defective auditory recognition after small hemorrhage in the inferior colliculi. *Journal of Neurological Sciences*, **161**, 91–96.

Johnsrude IS, Penhune VB and Zatorre RJ (2000). Functional specificity in right human auditory cortex for perceiving pitch direction. *Brain*, **123**, 155–163.

Kester DB, Saykin AJ, Sperling MR, O'Connor MJ, Robinson LJ and Gur RC (1991). Acute effect of anterior temporal lobectomy on musical processing. *Neuropsychologia*, **29**, 703–708.

Kinsella G, Prior MR and Murray G (1988) Singing ability after right and left sided brain damage. A research note. *Cortex*, **24**(1), 165–169.

Kohlmetz C, Muller SV, Nager W, Munte TF and Altenmuller E (2003). Selective loss of timbre perception for keyboard and percussion instruments following a right temporal lesion. *Neurocase*, **9**, 86–93.

Lechevalier B, Rossa Y, Eustache F, Schupp C, Boner L and Bazin C (1984). Un cas de surdit, corticale, pargnant en partie la musique. *Revue Neurologique*, **140**, 190–201.

Levin HS and Rose JE. (1979)Alexia without agraphia in a musician after transcallosal removal of a left intraventricular meningioma. *Neurosurgery*, **4**, 168–174.

Liegeois-Chauvel C, Peretz I, Babai M, Laguittin V and Chauvel P (1998). Contribution of different cortical areas in the temporal lobes to music processing. *Brain*, **121**, 1853–1867.

Lo YL and Fook-Chong S (2004). Ipsilateral and controlateral motor inhibitory control in musical and vocalization tasks. *Experimental Brain Research*, **159**(2), 258–262.

Mandell J, Schulze K and Schlaug G (2007) Congenital amusia: an auditory-feedback disorder? *Restorative Neurology and Neuroscience*, **25**, 323–334.

Marin OSM and Perry DW (1999) Neurological aspects of music perception and performance. In Deutsch D, ed. *Psychology of music*, 653–724. Academic Press, San Diego, CA.

Mavlov L (1980). Amusia due to rhythm agnosia in a musician with left hemisphere damage: a non-auditory supramodal defect. *Cortex*, **16**, 331–338.

Mazzoni (1993). A case of music imperception. *Journal of Neurology, Neurosurgery and Psychiatry*, 56, 322.

Mazzucchi A, Marchini C, Budai R and Parma M (1982). A case of receptive amusia with prominent timbre perception defect. *Journal of Neurology, Neurosurgery and Psychiatry*, **45**, 644–647.

McDonald C and Stewart L (2008) Uses and functions of music in congenital amusia. *Music Perception*, **25**(4), 345–355.

McFarland HR and Fortin D (1982) Amusia due to right temporoparietal infarct. *Archives of Neurology*, **39**(11), 725–727.

Mendez MF and Geehan GR (1988). Cortical auditory disorders:clinical and psychoacoustic features. *Journal of Neurology, Neurosurgery and Psychiatry*, **51**, 1–9.

Milner B (1962). Laterality effects in audition. In VB Mountcastle, ed., *Interhemispheric relations and cerebral dominance*, 177–195. Johns Hopkins University Press, Baltimore, MD.

Murayama J, Kashiwagi T, Kashiwagi A and Mimura M (2004). Impaired pitch production and preserved rhythm production in a right brain-damaged patient with amusia. *Brain and Cognition*, **56**, 36–42.

Patel AD, Peretz I, Tramo M and Labreque R (1998). Processing prosodic and musical patterns: a neuropsychological investigation. *Brain and Language*, **61**, 123–144.

Peretz I (1990). Processing of local and global musical information by unilateral brain-damaged patients. *Brain*, **113**, 1185–1205.

Peretz I (1996). Can we lose memory for music? A case of music agnosia in a non-musician. *Journal of Cognitive Neuroscience*, **8**, 481–496.

Peretz I, Coltheart M (2003). Modularity of music processing. *Nature Neuroscience*, **6**, 688–691.

Peretz I and Gagnon L (1999). Dissociation between recognition and emotion for melodies. *Neurocase*, **5**, 21–30.

Peretz I, Belleville S and Fontaine F (1997). Dissociations entre musique et langage apres atteine cerebrale; un nouveau cas d'amusie sans aphasie. *Canadian Journal of Experimental Psychology*, **51**, 354–368.

Peretz I, Blood AJ, Penhune V and Zatorre R (2001). Cortical deafness to dissonance. *Brain*, **124**, 928–940.

Peretz I, Brattico E and Tervaniemi M (2005). Abnormal electrical brain responses to pitch in congenital amusia. *Annals of Neurology*, **58**, 478–482.

Peretz I, Gagnon L and Bouchard B (1998). Music and emotion: perceptual determinants, immediacy, and isolation after brain damage. *Cognition*, **68**, 111–141.

Peretz I, Champod A-S and Hyde KL (2003). Varieties of musical disorders. The Montreal Battery of Evaluation of Amusia. *Annals of the New York Academy of Sciences*, **999**, 58.

Peretz I, Kolinsky R, Tramo M, Labrecque R, Hublet C, Demeurize G *et al.* (1994) Functional dissociations

following bilateral lesions of auditory cortex. *Brain*, **117**, 1283–1301.
Piccirilli M, Sciarma T and Luzzi S (2000). Modularity of music: evidence from a case of pure amusia. *Journal of Neurology, Neurosurgery and Psychiatry*, **69**, 541–545.
Prior M, Kinsella G and Giese J (1990). Assessment of musical processing in brain-damaged patients: implications for laterality of music. *Journal of Clinical and Experimental Neuropsychology*, **12**, 301–312.
Racette A, Bard, C and Peretz I (2006). Making non-fluent aphasics speak: sing along! *Brain*, **129**(10), 2571–2584.
Riecker A, Ackermann H, Wildgruber D, Dogil G and Grodd W (2000). Opposite hemispheric lateralization effects during speaking and singing at motor cortex, insula and cerebellum. *Neuroreport*, **11**, 1997–2000.
Robin DA, Tranel D and Damasio H (1990). Auditory perception of temporal and spectral events in patients with focal left and right cerebral lesions. *Brain and Language*, **39**, 539–555.
Samson S and Zatorre RJ (1988). Melodic and harmonic discrimination following unilateral cerebral excision. *Brain and Cognition*, **7**, 348–360.
Samson S and Zatorre RJ (1991). Recognition memory for text and melody of songs after unilateral temporal lobe lesion: evidence for dual encoding. *Journal of Experimental Psychology: Learning, Memory and Cognition*, **17**, 793–804.
Samson S and Zatorre RJ (1992). Learning and retention of melodic and verbal information after unilateral temporal lobectomy. *Neuropsychologia*, **30**, 815–826.
Samson S and Zatorre RJ (1994). Contribution of the right temporal lobe to musical timbre discrimination. *Neuropsychologia*, **32**, 231–240.
Samson S, Ehrle N and Baulac M (2001). Cerebral substrates for musical temporal processes. *Annals of the New York Academy of Sciences*, **930**, 166–178.
Samson S, Zatorre RJ and Ramsay JO (2002). Deficits of musical timbre perception after unilateral temporal-lobe lesion revealed with multidimensional scaling. *Brain*, **125**, 511–523.
Satoh M, Takeda K, Murakami Y, Onouchi K, Inoue K and Kuzuhara S (2005). A case of amusia caused by the infarction of anterior portion of bilateral temporal lobes. *Cortex*, **41**, 77–83.
Schön D, Lorber B, Spacal M and Semenza C (2004). A select deficit in the production of exact musical intervals following right hemisphere damage. *Cognitive Neuropsychology*, **21**, 773–785.
Schuppert M, Munte TF, Wieringa BM and Altenmuller E (2000). Receptive amusia: evidence for cross-hemispheric neural networks underlying music processing strategies. *Brain*, **123**, 546–559.
Shankweiler D (1966). Effects of temporal lobe damage on the perception of dichotically presented melodies. *Journal of Comparative Physiology and Psychology*, **62**, 115–119.
Shapiro BE, Grossman M and Gardner H (1981). Selective musical processing deficits in brain damaged populations. *Neuropsychologia*, **19**, 161–169.
Sidtis JJ and Volpe BT (1988). Selective loss of complex-pitch or speech discrimination after unilateral lesion. *Brain and Language*, **34**, 235–245.
Sloboda JA, Wise KJ and Peretz I (2005). Quantifying tone deafness in the general population. *Annals of the New York Academy of Sciences*, **1060**, 255–261.
Spreen O, Benton AL and Fincham RW (1965). Auditory agnosia without aphasia. *Archives of Neurology*, **13**, 84–92.
Stewart L, Overath T, Warren JD, Foxton JM and Griffiths TD (2008) fMRI Evidence for a cortical hierarchy of pitch pattern processing. *PLoS ONE*, **3**(1), e1470. doi:10.1371/journal.pone.0001470.
Stewart L, Von Kriegstein K, Warren JD and Griffiths TD (2006) Disorders of musical listening. *Brain*, **129**, 2533–2553.
Stewart L, Walsh V, Frith U and Rothwell J (2001). Transcranial magnetic stimulation produces speech arrest but not song arrest. *Annals of the New York Academy of Sciences*, **930**, 433–435.
Tanaka Y, Yamadori A and Mori E (1987). Pure word deafness following bilateral lesions. *Brain*, **110**, 381–403.
Terao Y, Mizuno T, Shindoh M, Sakurai Y, Ugawa Y, Kobayashi S *et al.* (2005) Vocal amusia in a professional tango singer due to a right superior temporal cortex infarction. *Neuropsychologia*, **44**, 479–88.
Tramo MJ and Bharucha JJ (1991). Musical priming by the right hemisphere post-callosotomy. Neuropsychologia, 29, 313–325.
Tramo MJ, Bharucha JJ and Musiek FE (1990). Music perception and cognition following bilateral lesions of auditory cortex. *Journal of Cognitive Neuroscience*, **2**, 195–212.
Tramo MJ, Shah GD and Braida LD (2002). Functional role of auditory cortex in frequency processing and pitch perception. *Journal of Neurophysiology*, **87**, 122–139.
Ustvedt HI (1937). Ueber die Untersuchung der musikalischen Funktionen bei Patienten mit Gehirnleiden besonders bei Patienten mit Aphasie. *Acta Medica Scandinavica*, **86**, 1–186.
Warrier CM and Zatorre RJ (2004). Right temporal cortex is critical for utilization of melodic contextual cues in a pitch constancy task. *Brain*, **127**, 1616–1625.
Wilson SJ, Pressing JL and Wales RJ (2002). Modelling rhythmic function in a musician post-stroke. *Neuropsychologia*, **40**, 1494–1505.
Yamadori A, Osumi Y, Masuhara S and Okubo M (1977) Preservation of singing in Broca's aphasia. *Journal of Neurology, Neurosurgery and Psychiatry*, **40**(3), 221–224.
Zatorre RJ (1984). Musical perception and cerebral function: A critical review. *Music Perception*, **2**, 196–221.
Zatorre RJ (1985). Discrimination and recognition of tonal melodies after unilateral cerebral excisions. *Neuropsychologia*, **23**, 31–41.
Zatorre RJ (1988). Pitch perception of complex tones and human temporal-lobe function. *Journal of the Acoustical Society of America*, **84**, 566–572.
Zatorre RJ and Halpern AR (1993). Effect of unilateral temporal lobe excision on perception and imagery of songs. *Neuropsychologia*, **31**, 221–232.
Zatorre RJ and Samson S (1991). Role of the right temporal neocortex in retention of pitch in auditory short-term memory. *Brain*, **114**, 2403–2417.