Variations on the musical brain

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If intelligent extraterrestrials ever intercept *Voyager*, the first message they decode will be Glenn Gould playing Bach[1]. Music, an ancient and peculiarly human pastime, is valued by all cultures. For highly visual primates, we are surprisingly susceptible to these abstract acoustic stimuli with no obvious survival value[2]. Neurologists have long been fascinated by musical curiosities they occasionally meet in their clinical practice. With the advent of techniques such as functional magnetic resonance imaging (fMRI), positron emission tomography (PET) and transcranial magnetic brain stimulation (TMS) it has become possible to study the perception and production of music in detail. A brief set of variations may serve to outline the theme.

ANATOMY OF MUSIC PERCEPTION

Figure 1 is a tentative schema of the anatomy of music perception, derived from PET, fMRI and lesion data[3–6]. Processing of the raw acoustic signal begins in the ascending auditory pathways—a hierarchy of brainstem structures that terminate in the primary auditory cortex on the first temporal convolution. The cortical representation of frequencies forms a 'tonotopic' map. Components of the musical stimulus are distributed to adjoining association areas in the temporal lobe, and to more remote regions spanning the cortical mantle. The total conscious experience of music is the result of activity in widely distributed brain areas, which form 'neural networks' dedicated to particular aspects of musical processing. Analysis of fine structure in time (rhythm) and space (pitch intervals on a mental stave) occurs mainly in the left hemisphere, while colour (timbre) and contour (melody) are processed mainly in the right. Identification of familiar compositions, which probably in part requires the brain to assign a verbal 'tag' to the music, is predominantly a left hemisphere function[5]. Metre does not show hemispheric lateralization[4,6]. Judgments of familiarity and timbre, which probably call upon the brain's total experience of musical form and colour respectively, activate corresponding areas at the frontal pole in opposite hemispheres[5]. A high degree of overlap occurs between the areas coded in Figure 1. The fundamental interhemispheric division of labour may lie between pitch (interval, contour) and time signature (rhythm, metre) information. However, the key elements of musical processing (pitch, rhythm, melody, timbre) remain surprisingly difficult to define, isolate and study. The brain may treat these elements as specific examples of more general cognitive tasks. A patient with disturbed recognition of rhythm, for instance, may fail to perceive rhythmic patterns in auditory, visual or tactile domains[7]. Subcortical structures, such as the thalamus, may stabilize networks that generate auditory images[8]. Other deep structures, notably the limbic system, confer on auditory stimuli their emotional tone (see below).

Plasticity is a property of all levels of the auditory system. Musical training promotes the use of analytical strategies for processing fine structure (left hemisphere), whereas musically untrained listeners principally respond to the overall contour and 'colour' of music (right hemisphere)[9]. Increased right hemisphere blood flow accompanies perception of harmony (but not rhythm) in non-musicians, whereas musicians show increased left hemisphere blood flow with both types of stimulus[10]. Right hemisphere lateralization may be modulated by several factors: it is more evident in females and non-attentive listeners at all levels of musical training[10]. Hemispheric dominance may also be influenced by culture: Japanese folk music, for example, is processed primarily in the left hemisphere by native Japanese, in the right hemisphere by Westerners[11]. Although the role played by hemispheric specialization in human cognitive evolution has received due recognition[2], broad generalizations about hemispheric dominance neglect the crucial role of hemispheric interdependence. Thus the brain is unable to extract information regarding pitch intervals (left hemisphere) without an intact melody processor (right hemisphere), probably because it lacks the anchoring points necessary to judge intervals when contour information is missing[4].

CLINICAL IMPAIRMENTS OF MUSICAL FUNCTION: THE AMUSIAS

Like language, music has a vocabulary (notes, musical phrases), syntax (scales, melodies), grammar ('rules' of composition) and notation (the score). A complex musical task such as sight-reading activates a brain network parallel to, but distinct from, the network for verbal processing[12]. Spoken language frequently relies on prosody—the stresses, rhythms and pitch changes which compose the 'melody' of speech—to convey meaning[2,13]. Brain lesions may destroy certain components of the musical experience while leaving

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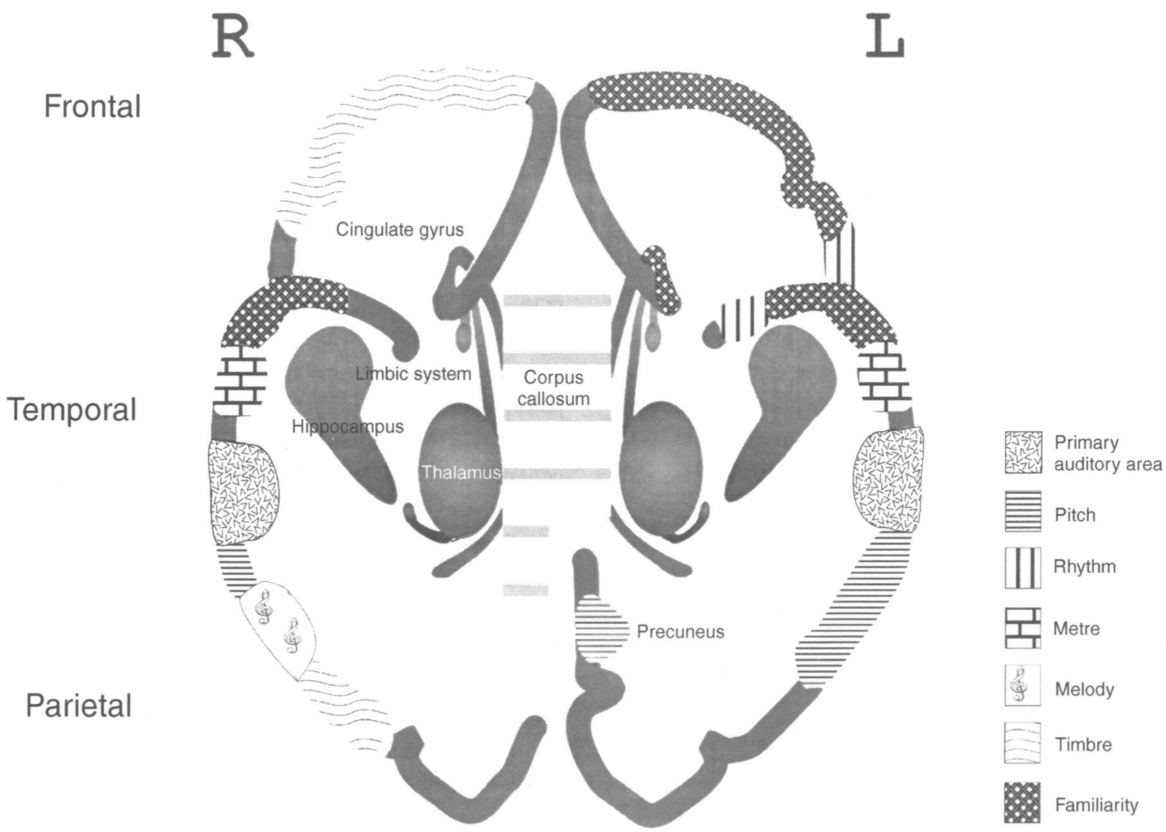

Figure 1 **Schematic axial slice of the human cerebral hemispheres, showing structures involved in music perception.** Key areas involved in processing each component of the musical stimulus are coded at the right of the figure. These areas form interdependent neural networks, rather than 'centres' where particular functions are localized.

others intact, and parallels to the aphasias (expressive and receptive) exist for music: the amusias[14]. The most famous sufferer was Ravel, who developed a degenerative illness (possibly Pick's disease) which selectively destroyed his ability to express musical ideas, although his comprehension remained as keen as ever[15]. Benjamin Britten's stroke, which affected language but appeared to spare his musical faculties, is one celebrated example of dissociated verbal and musical processing[3,16]. Patients with a stroke that severely impairs the fluency of spoken language may still be able to sing effortlessly, and the reverse pattern, though less common, is also well recognized[2,3,13]. However, in many cases, verbal and musical deficits are produced by the same insult, generally in the left hemisphere, and the occurrence, type or severity of amusia cannot be predicted on the basis of a single brain lesion[3]. Inability to recognize rhythm or pitch contour, for example, might have quite diverse anatomical implications[7] (see Figure 1).

SYNAESTHESIA

The phenomenon of synaesthesia, or 'coloured hearing', has been recognized since at least 1690, when John Locke described 'a studious blind man who bragged one day that he now understood scarlet was... the sound of a trumpet'[17]. The sounds that provoke synaesthesia are most commonly words, but musical tones may also trigger the experience. The correspondence between sounds and the colours they evoke is determined by the individual brain. True synaesthesia is concrete, external, involuntary, reproducible from day to day, typically lifelong, and probably inherited[17,18]. It is more common in women. Some synaesthetes have subtle evidence of left hemisphere dysfunction, but an eidetic memory is also a frequent accompaniment[18]. Synaesthesia may occur in seizures arising from the temporal lobe. Scriabin, Sibelius, Rimsky-Korsakov and Messiaen were probably synaesthetes: to Rimsky-Korsakov C major seemed white, to Scriabin red; both reported that E major was blue, A flat major purple, and D major yellow[19]. PET studies of coloured hearing demonstrate activation of colour processing areas in response to words[17]. These areas normally associate perceptions of colour with other features of a visual stimulus, such as shape. Synaesthesia may thus be a variant of normal brain activity.

MUSICAL HALLUCINATIONS, MUSICOGENIC EPILEPSY AND THE TEMPORAL LOBE

Musical hallucinations[20] may arise without any evidence of psychiatric illness, driving the patient to distraction by the continual repetition of some usually banal melody or theme that lacks any personal significance. Often hallucinations arise in the context of hearing impairment, and some degree of abnormal central disinhibition is probably also required. They may occur after brain damage (especially right hemisphere) or with temporal lobe seizures. The experience of hearing music is commonly reported after electrical stimulation of cortical areas, in either temporal lobe[21]. Stimulation of the primary auditory area itself elicits crude acoustic impressions such as buzzing, rather than music. This further suggests that the conscious experience of music, in contrast to elemental sounds, emerges from the synthesis of activity in other brain areas. Musical and other memories reconstituted by external stimulation or seizure activity have a characteristic emotional tenor. This marriage of intellect and emotion, a primary function of the normal temporal lobe, is accomplished by intimate anatomical and functional connections between temporal cortex, hippocampus and limbic structures (see Figure 1 and below). A further dimension is suggested by the peculiar aversion some people have for particular musical tones and timbres, such as Mozart for the trumpet[22]. Very rarely, singing may occur as an epileptic automatism; one such patient had a seizure focus in the right temporal lobe[23]. This is presumably an instance of a seizure discharge releasing fragments of a musical motor programme.

Occasionally, music provokes seizures—so-called musicogenic epilepsy[24]. The stimulus may be a peculiar combination of tones (for example, church bells), but in other cases a degree of emotional involvement seems to be required[25]. In one case seizures were provoked by listening to 'sentimental light music'[11]. Even the act of recalling music is sufficient provocation in some sufferers. Musicogenic seizures may arise from either temporal lobe[24,25]—further circumstantial evidence of the bilaterality of musical processing.

NEUROLOGY OF PERFECT PITCH

Absolute or 'perfect' pitch, the ability to identify a given note in the absence of a pitch reference, may signify that the brain has a stable fixed pitch template[26,27]. Possessors refer to the unique qualities of particular tones, which seem independent of the octave. PET evidence suggests that visual imagery of a musical stave is used by some musically untrained subjects in a pitch discrimination task[5], and a vivid musical imagination probably makes use of mental imagery in various non-auditory domains: Jacqueline du Pré was able to play by visualizing the positions of her fingers on the cello, even when tactile feedback was distorted by the lesions of multiple sclerosis[28]. Similar multimodality imagery, possibly involving strategically placed cortical association areas such as the precuneus[29] (see Figure 1), may help maintain absolute pitch[30]. Both genetic and environmental factors contribute to its development[31] and it is usually associated with intensive musical exposure in early life. The pitch reference may be shifted by brain lesions[32], normal ageing and the menstrual cycle[33]. The left *planum temporale* is enlarged in some musicians with perfect pitch[34], but the effects of lesions in this and other brain areas have been inconsistent[32].

MUSICIAN'S CRAMP—A FOCAL DYSTONIA

The dystonias are distinguished by sustained patterns of muscle contraction and posturing. Many 'task-specific' or occupational dystonias are recognized; writer's cramp is the commonest[35]. Musicians are over-represented, and various forms of painless 'musician's cramp' have been described[36–38]. Robert Schumann probably had a form of the condition afflicting his right hand[39]. It may strike quite different muscle groups, such as those forming the embouchure in wind players[38].

Normal cerebral activity is the sum of excitation and inhibition in a very large number of neural circuits. The basal ganglia play a crucial role in setting the balance of cortical excitation and inhibition[40], and an alteration in this balance may permit dystonia to develop. Like the networks involved in music perception, those responsible for musical movement planning seem to be 'plastic', susceptible to reprogramming by physiological and occupational influences, including intensive musical training. High-fidelity processing of *sensory* information is essential for normal motor control. Gordon Holmes expressed this in a musical analogy:

> 'The motor cortex cannot be compared with the keyboard of . . . a musical instrument, in which a constant result is obtained on striking each key. The response of each motor point to adequate stimulation is not fixed or immutable; it may be modified by various factors and particularly by previous activity of itself or of a neighbouring point'[41].

Cortical representations of the fingers of the left (but not the right) hand in skilled string players are larger and shifted on the cortex compared with those of musically untrained subjects[42]. Enlargement of the cortical representations of piano tones is also seen in trained musicians[43]. Both effects correlate with the age at which the person began to play. Such observations are strong circumstantial evidence that functional reorganization of both sensory and motor cortex can be use-dependent. Plastic maps, such as those established by musical and other forms of occupational activity, may be susceptible to abnormal reorganization by repetitive sensory feedback. TMS maps of individual hand muscles[44] are shifted and distorted in patients with writer's cramp relative to normal subjects. However, the abnormal map can be returned to a more normal position by the therapeutic use of botulinum toxin[44]. Cortical sensory representations of the fingers are disordered in patients with hand dystonia[45], providing a further link in the proposed chain of events whereby abnormal sensory inputs give rise to abnormal motor maps. The motor cortex is more excitable[46] and there is less inhibition between the hemispheres[47] in patients with task-specific dystonia, including musician's cramp, than in normal subjects. The final common pathway of many genetic and environmental factors may be a deficiency of cortical inhibition[40].

MUSIC AND THE NEUROLOGY OF EMOTION

Perhaps the most extraordinary property of music is its ability to conjure surrogate emotions. The physiological correlates of intense absorption in music are very similar to those of 'real' emotions, implying shared neural mechanisms: in the famous case of Herbert von Karajan, blood pressure and heart rate fluctuations while he conducted a Beethoven symphony were similar to those when he was landing a jet aircraft[24]. The general agreement among listeners (at least those sharing a common cultural milieu) regarding the emotions engendered by many musical works is further evidence that they occupy a neural common ground. Even within a single musical fragment, the response can be surprisingly uniform and very precise; the return of the bass voice in the fifteenth Goldberg, for instance, remains the emotional centre of gravity of that variation even after repeated hearings. Limbic circuits normally weld physiological responses to the cognitive content of emotionally laden stimuli such as music. Perversions of limbic activity may take dramatic forms, such as musical hallucinations and epilepsy (see above). In a musically trained patient awaiting epilepsy surgery, hippocampal responses to consonances and dissonances were shown to be partitioned as a function identical to the relation between the same intervals in the well-tempered tuning of two-voice counterpoint[48]. The pattern was specific for the hippocampus, a key brain component in memory and emotion. This is a striking example of brain organization mirroring mathematical music theory, and may represent a substrate for the emotional immediacy of complex musical structures[2].

CODA

While many details remain obscure, a broad appreciation of the musical brain is now possible. In order for sounds to be perceived as musical, the auditory stimulus is first decomposed, and each component distributed in a coordinated manner to the widespread cortical areas adapted for recovering the type of information (rhythmically repeating patterns, symbols in a visuospatial array, contours) it encodes. These cortical sketchings are given colour and poignancy by the participation of deep temporal and limbic structures, which recruit the ancient physiological apparatus of the 'fight or flight' response as they unlock the individual memories forming the brain's own record of past experience. Reunification of these diverse elements into a coherent conscious experience probably depends on structural and functional properties of temporal cortex which remain poorly understood. If the listener is also a performer, the machinery of perception is subverted to the planning and execution of the motor programme for the musical task, which relies on detailed moment-to-moment communication between sensory and motor networks embracing a matrix of cortical and subcortical structures. All of these networks may be modified by physiological, pathological and cultural influences.

On the one hand, music is the product of a human brain, and seems to require similarly structured brains to apprehend it. On the other, there is a sense in which music, like mathematics, reflects the fundamental structure of the physical world, perceived and created by us because our brains are also part of that world. Extraterrestrials happening upon the first prelude of the '48' will no doubt deduce that it is the artefact of another mind; but will they find it beautiful?

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