IN A NUTSHELL

- Pitch is the **basic building block** for music.
- **People with amusia** – extreme tone deafness – **cannot detect pitch patterns.**
- Amusia may be caused by **defective connections between the frontal and temporal lobes.**
- **Overactivity in the brain** that allow us to perceive or imagine music **may cause musical hallucinations.**

FEATURES

~~Manchu memoirs~~

~~The genetic legacies of the Manchus in China (such as Manchu statesman Shen Kwe-fen, photographed in 1860) and of Mongol supreme Genghis Khan are being uncovered by Chris Tyler-Smith, who moved from Oxford University to the Wellcome Trust Sanger Institute to apply high-throughput genetics to the study of human evolution.~~

LOST IN TONE

Music and the brain

For people with amusia, an extreme form of tone deafness, or musical hallucinations, where the same tune is heard over and over, music is a joyless experience. Using behavioural tests and modern imaging techniques to illuminate the brain's workings, Tim Griffiths has found that the brains of people with tone deafness and musical hallucinations process complex musical sounds differently from the rest of us. The relevance of the work extends beyond the musical domain.

Our ability to play or even appreciate music can vary markedly. Everyone knows someone who cannot carry a tune and was banned from the school choir. But people with amusia go far beyond bad singing in the shower: they are so tone-deaf that they can't recognise familiar tunes or distinguish between two melodies at all, no matter how different. Mahler sounds the same as Madonna, the Gorillaz the same as God Save the Queen. And while most people can tell when they are off key, amusic people cannot hear how badly they sing unless someone tells them.

"For these people music is nonsensical. Some of them even find it irritating," says Professor Tim Griffiths, a Wellcome Trust Senior Clinical Fellow investigating this musical disorder at the University of Newcastle upon Tyne and the Wellcome Department of Imaging Neuroscience, University College London (UCL). "It's a surprisingly common problem: amusia affects up to 5 per cent of the population." Famous people such as US President Theodore Roosevelt and the revolutionary Che Guevara suffered from this musical impairment.

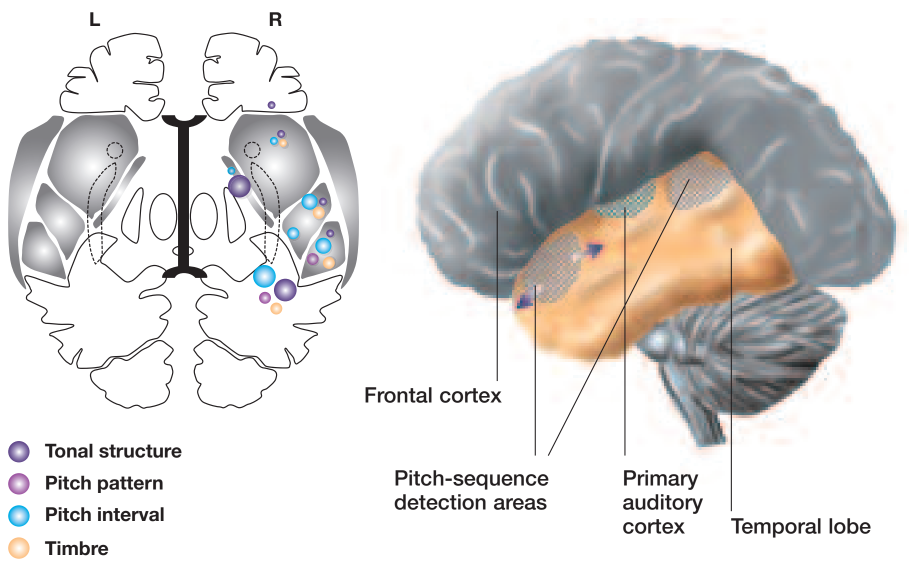
For neuroscientists the condition is particularly fascinating because it is specific to music. In every other way, amusic people are perfectly normal: they have no history of neurological or psychiatric disorder and were exposed to music as children; the problem is not in their hearing, as they perceive other sounds perfectly well; and they have no difficulties with languages or in recognising familiar voices. But when it comes to music, however, it can all sound like noise – one amusic individual describes Rachmaninov's second piano concerto, which can reduce people to tears, as "banging that would be best avoided".

Pitch pathways

The key problem for people with amusia is pitch – the basic building block for music, as melodies are patterns of pitch. Somewhere, the pathways in the brain that process pitch are impaired. To shed light on what neural networks are affected, Professor Griffiths and his team are looking at how the brains of individuals with and without amusia process musical stimuli.

First, the researchers must identify whether a person is amusic or not. A simple test developed by Montreal University researchers does the job in minutes. Volunteers are asked to listen to pairs of musical phrases and say whether or not the tune has changed.

PITCH IMPERFECT



Left: Common sites of acquired brain damage (usually stroke) that can cause abnormalities of the systems for melody and timbre. Other sites can affectthe brain1s processing of the time interval, rhythm or emotion of music, ordisrupt the recognition of whether a melody is new or familiar.

Right: Signals from the ear are transmitted via the auditory nerve to the primary auditory cortex in the temporal lobe, where certain cells are sensitive to specific frequencies. To process music, however, additional areas of the brain are needed: simple patterns (sequences) of pitch are analysed in local networks within the temporal lobes, while the analysis of the overall Œexperience1 of music requires distributed networks in the frontal cortex and temporal lobe.

Sometimes the melodies are identical, other times they have been altered by inserting a wrong note. It's a 'spot the difference' with sounds. (Take the online test at www.delosis.org.)

Amusic people are bad at detecting these differences: "It's amazing that people with this condition can't do this test at all," says Professor Griffiths. "In Newcastle, we have used the tests developed in Montreal for the detection of altered melodies, and tests we have developed for the detection of simple differences between pairs of notes. We have identified a problem in amusia with the detection of whether notes go up or down. This is a 'building block' for contour – the pattern of 'ups' and 'downs' in pitch during a melody. So it looks as if the problem in amusia is a fundamental deficit in the analysis of pitch patterns that are especially relevant to music."

Which mechanisms in the brain are going wrong in amusia? To help find out, Professor Griffiths has been working with normal subjects at UCL's Wellcome Department of Imaging Neuroscience, using functional magnetic resonance imaging to map the brain areas that are activated while the volunteers listen to pitch patterns including melodies.

These studies suggest that there is a hierarchal organisation to the analysis of melody. The pitch of individual notes is represented in the brain in 'pitch centres' in the temporal lobes. Simple patterns of pitch, such as short atonal melodies, are analysed in local networks within the temporal lobes. At higher levels of 'musical cognition', such as the analysis of the tonality of a piece, the networks for analysis become even more distributed and involve the frontal cortex as well as the temporal lobes.

As amusic people have a problem with pitch direction, this suggests that the brain deficits go beyond the 'pitch centre' for the analysis of the pitch of individual notes. In a recent collaboration with Isabelle Peretz of Montréal University in Canada, the Newcastle researchers used a technique called voxel-based morphometry to directly examine this hypothesis. The technique uses magnetic resonance imaging to measure the density of white matter in the brain. (White matter is made up of nerve cell processors or axons that carry nerve impulses between the cortical areas in which computational processing is carried out.)

The researchers found that the white matter connecting the right frontal lobe with the auditory cortex in the right temporal lobe is thinner in amusic people than in musically able subjects. The problem in amusia may therefore be a connectivity glitch: "The connectivity problem gets worse as the tone deafness gets worse," says Professor Griffiths. "This suggests that in people with amusia, the networks for melody analysis that depend on connections between the frontal and temporal lobes are disrupted."

But what is the cause of this remarkable music-processing deficit? Amusia seems to run in families: as far back as 1925, geneticists found evidence for the heritability of pitch discrimination. Professor Griffiths and his colleagues Lauren Stewart in London and Patrick Chinnery (another Wellcome Trust Senior Clinical Fellow) in Newcastle are assessing families in which several members are affected. "Supposing we were able to identify a particular gene that causes this miswiring, such as that encoding a cell adhesion molecule, then it might have relevance to a broader range of disorders," he says. "The disorder is interesting because of its specificity for music, but it might also be a model system for other disorders in which abnormal connectivity has been implicated, such as schizophrenia."

History repeating

Many of us have a 'tune in our head' for an hour or a day, perhaps prompted by a song on the radio in the morning or by someone whistling. But people with musical hallucinations hear music all the time – to such an extent that it becomes intrusive. It might be a hymn, a pop tune, Three Blind Mice or Edelweiss playing constantly. Yet there is no music. It's a hallucination: they are not imagining the music – it is not their 'inner voice' – but are hearing it over and over, day after day. This untreatable, distressing and debilitating condition mostly affects middle-aged and elderly individuals who have become deaf, although it can be triggered by epileptic seizures, brain tumours or psychosis.

Doctors have long known about musical hallucinations. The German composer and pianist Robert Schumann is a famous example. Towards the end of his life he had musical hallucinations that evolved from simple experiences (hearing an A note) to hearing complex orchestral music. Some of his grandiose descriptions – such as one of hearing "an instrument of splendid resonance, the like of which has never been heard on Earth before" – are consistent with bipolar affective disorder, but there is still debate about whether he had neurosyphilis. Whether the condition was ever actually helpful in his work and life is uncertain, but this is never the case in the common variety of musical hallucination in association with deafness. The music they have stuck in the brain is usually something they heard before they became deaf.

The phenomenon is a little like tinnitus, in which subjects may hear a simple tone or noise, but differs in its complexity. Certain models for tinnitus have been based on overactivity in the auditory cortex. Professor Griffiths believes that musical hallucinations could be the result of overactivity in the more widely distributed brain networks that normally allow us to perceive or imagine music. He has used a scanning technique known as positron emission tomography to study the brains of people who have developed musical hallucinations, and has found a network of regions in the brain that become more active when the hallucinations become more intense. This is a similar pattern to that found in normal people who are listening to music.

"Musical hallucinations are an amplification of a normal mechanism," he says. The main difference from actually listening to music is that the hallucinations only use the parts of the brain in which activity correlates with the perception of melody, and not the whole auditory pathway from the ears. In normal people, any tendency to abnormal activity in this perceptual network is suppressed by the constant stream of information from the ears. In deaf people, that acoustic censorship is gone, and the result is false music.

"It is the same network that might be responsible for thinking about a tune and getting that tune stuck in the head. But it is different [in a musical hallucination] in that it is very real." In fact, when the false music first happens, subjects almost invariably think that there is a band playing next door or that someone has the radio on loud.

The disorder is very difficult to treat – a mainstay of therapy is improving people's hearing aids. Many therapies have proved to be unhelpful, although the group is interested in exploring the use of certain drug treatments that have been evaluated in tinnitus.

Wobbly divas

As a neurologist, Professor Griffiths hopes to translate his basic science discoveries into clinical applications. The systematic hearing tests for tone deafness, he believes, could become a more general tool for studying auditory cognition in a wide range of disorders. "I'm keen to use some of these measures to get a handle on brain processing in other common disorders," he says. "The measures we are developing allow us to test the integrity of widely distributed cortical mechanisms that might be affected by disorders such as autism and schizophrenia, and not just problems with musical perception."

For example, existing tests for autism are visual tests that pinpoint the excessive attention to detail in these subjects, or inability to 'see the wood for the trees'. Would it be possible to develop a similar test based on auditory cognition? His team, in collaboration with Lauren Stewart and Uta Frith at UCL, has been using a test inspired by wobbly opera singers. "If you listen to a soprano, you might hear her singing with a 'vibrato' to carry her voice over the orchestra, where the pitch goes up and down all the time instead of holding the same note." In the clinical test the 'wobble' rate can be altered, and people must say when they detect a change in the pattern. It is a way of assessing the ability to detect a higher-order pattern (the change in rate of wobble) over and above the wobble itself: an auditory equivalent of 'seeing the wood for the trees'.

Music is important to us – our brain is primed for music. A greater understanding of how our brains process music, and the biological basis of both musical perception and processing deficits, could tell us much about what makes humans tick.

GLOSSARY

Pitch: The perceived highness or lowness of a tone

Contour: A pattern of 'ups_ and 'downs_ in pitch during a melody

Melody: A succession of single tones or pitches that form a distinctive sequence

Timbre: The quality of a sound that distinguishes one voice or musical instrument from another

By Lisa Melton, a science writer based in London.

Further reading

Foxton JM et al. Characterization of deficits in pitch perception underlying 'tone deafness'. Brain 2004;127(4):801–10.

Foxton JM et al. Rhythm deficits in 'tone deafness'. Brain Cogn 2006;62(1):24–9.

Griffiths TD. Musical hallucinosis in acquired deafness. Phenomenology and brain substrate. Brain 2000;123(10):2065–76.

Hyde KL et al. Morphometry of the amusic brain: a two-site study. Brain 2006;129(10):2562–70.