Spatial and temporal mapping of neural activity associated with auditory hallucinations

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Auditory hallucinations are a common and distressing symptom of psychosis. The underlying pathophysiology is poorly understood. It is hypothesised that they arise from areas of auditory cortex subserving language. New functional imaging techniques can further our understanding, as they are well suited to exploring episodic phenomena. However, the unpredictable timing of hallucinations, along with the level of disturbance in the patients, make direct-observation methodologically difficult. Many investigators therefore use more indirect approaches, with consequent variability of results. We report a case of a male subject with schizophrenia who experienced a stable pattern of hallucinations such that we were able to take images of repeated episodes of hallucination and demonstrate the functional anatomy and time course of his psychotic phenomena.

Our patient was a 26-year-old right-handed male with an 8-year history of paranoid schizophrenia, on stable medication. He gave written informed consent, and local ethics committee approval was obtained. He pressed a button to indicate the start and end of the hallucination. Scanning was done at the University of Nottingham Magnetic Resonance Centre using a 3 Tesla magnet (Oxford Magnet Technology), purpose-built head gradient set and birdcage quadrature radiofrequency coil. Continuous, whole brain T2 coronal echoplanar images were taken (TR 250 ms/slice, TE 26 ms, matrix size 128×64×12 voxels, voxel size 3×3×15 mm). Image processing and statistical analysis were performed using SPM96. This involved the realignment of the images to a mean image to correct for movement, normalisation into a standardised stereotactic space, and smoothing with a 5 mm isotropic Gaussian kernel.

The patient’s pattern of hallucinations was that a male voice would speak to him for on average 26 seconds, and then be silent for the same time. The data were analysed by subdividing the episodes of hallucination into seven sequential stages relating to the button presses. Contrasts were then created between each of the stages and the mid off period using box-car functions to give a series of images describing the evolution of the auditory hallucination over time. Significance of condition-specific effects was assessed using SPM(Z), and results displayed on a right view of a rendered brain, thresholded at p=0.001.

Activation first appeared in the three-second epoch before the on press in the right middle temporal gyrus. This activation was consistently present throughout the experience of the hallucination. Primary motor–cortex activations were present relating to the on and off press. Activation also extended in the early phase of the hallucination to a wider area of the right superior temporal and left superior temporal gyri, right middle and inferior frontal gyri, right anterior cingulate, and right cuneus.

These results show the strong association of the right middle temporal gyrus with the experience of auditory hallucination in this patient, supporting the hypothesis that auditory hallucinations reflect abnormal activation of auditory cortex. Language is more associated with the left hemisphere in normal subjects. This finding may therefore reflect the abnormal lateralisation of language function in schizophrenia. However, the right hemisphere is associated with emotional tone of speech, as well as auditory association. The rightsided activation shown in this patient, together with the activation of lateral prefrontal and cingulate areas, which are related to emotional memory and arousal, could therefore indicate the retrieval of emotional verbal memory during hallucination. This would reflect the nature of the auditory hallucinations experienced. The lack of left dorsolateral prefrontal cortex activation, an area associated with an internal monitor role, could explain why these activations are then misinterpreted as alien.

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