University of Sheffield, and were analysed using statistical parametric mapping (SPM). The fixed effect analysis (corrected for multiple comparisons) showed BOLD signal in patients with schizophrenia in left superior temporal gyrus and right medial frontal gyrus. We correlated an estimate of the magnitude of the BOLD response with performance on neuropsychological tests of verbal fluency across subjects (Letter Fluency, Category Fluency and Category Switching). Category Switching performance correlated positively with left superior temporal gyrus (-55 4 0) activation; and, negatively with right medial frontal gyrus (10 50 -4) activation. Letter Fluency and Category Fluency did not correlate with selected brain regions. These findings suggest that impairments in complex semantic processing and cognitive flexibility are mediated by brain mechanisms that are also involved in abnormal empathic reasoning in schizophrenia.

SCHIZOPHRENIA PATIENTS FAIL TO ACTIVATE NEURAL SUBSTRATES THAT ARE CRITICAL FOR COMPUTATION OF OUTCOME SUCCESS AND REWARD MAGNITUDE DURING DECISION-MAKING

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Decision-making is an important function of daily life and depends on a number of factors. For example, history of success and failure are important determinants for the selection of a response in a decision-making situation. Moreover, information regarding outcome and reward significantly affects the selection of the response. Schizophrenia patients show decision-making dysfunctions, however, the nature of these decision-making dysfunctions is unclear. Previous studies have shown that schizophrenia patients process the history of success and failure similar to normal comparison subjects but are unable to adequately process the uncertainty associated with the outcome of a response. This study examined the hypothesis that schizophrenia patients, who have previously shown altered parietal function associated with processing the uncertainty associated with an outcome of a response, will show altered parietal activation associated with processing the likelihood of success. 14 Schizophrenia patient and 14 normal comparison subjects participated in this study. All subjects performed the modified two-choice prediction task during functional magnetic resonance imaging (fMRI). For the modified two-choice prediction task, the subject is given additional information prior to making a decision. First, a set of stimuli indicates the likelihood of success when selecting a response. Second, numbers are shown, which indicate how many points the subject will win or lose if the prediction is correct. The goal for the subject is to gain as many points as possible. Each trial is self-paced, thus once the subject selects a response, the result is shown briefly (300 msec), and a new trial begins immediately thereafter. FMRI scanning was performed using a Siemens 1.5 Tesla scanner (FOV 64x64, TR 3.0 sec, TE 34 msec, 32 slices of 43 mm voxels were obtained for 128 repetitions). As hypothesized, schizophrenia patients showed significantly less activation in the posterior parietal cortex, i.e. the superior/inferior parietal lobule, precuneus, and the superior temporal gyrus during the modified two-choice prediction task. In contrast, schizophrenia patients relative to normal comparison subjects showed increased activation in left medial and superior frontal gyrus. In combination, these results support the conclusion that schizophrenia patients do not appropriately process outcome success and reward magnitude during decision-making.

EFFECT OF SCHIZOPHRENIA ON FRONTOTEMPORAL ACTIVITY DURING WORD ENCODING AND RECOGNITION: AN EVENT-RELATED FMRI STUDY

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Neuropsychological studies have shown that patient deficits in verbal episodic memory occur primarily during encoding, with relative sparing of long-term storage and non-relational recognition performance. Our previous positron emission tomography (PET) study found that this performance pattern was reflected by disrupted left frontotemporal activation and relatively intact right prefrontal activity. The current study extends this investigation to functional magnetic resonance imaging (fMRI). The Penn Word Recognition Test (PWRT) was administered to 11 patients with schizophrenia and 13 demographically balanced controls. Images were motion corrected, Talairach transformed, and spatially smoothed. An unbiased multiple regression procedure estimated the hemodynamic response, and a two-stage random effects model was used to investigate group differences. Resulting SPM{Z} maps were Bonferroni corrected (Z=3.6; p<.05, corrected) for the number of resels in the brain using the theory of Gaussian fields. There was no difference between patient (77 +/- 10 %correct) and control performance (86 +/- 13 %correct). Encoding results were similar to previous PET findings in that controls showed greater activation in left prefrontal (BA 9/46), right middle temporal (BA 22) and right inferior parietal regions (BA 40). Patients showed relatively greater activation in the amygdala. Recognition results varied from previous findings in that there was evidence of right superior frontal (BA 9) dysfunction in patients in addition to reduced activation in the right inferior temporal gyrus (BA 37). Patients did not show any areas of greater activation during recognition. These results underscore the central contribution of left frontotemporal dysfunction to impaired word encoding in schizophrenia. However, these results also bring into question previous claims that the right anterior prefrontal cortex is relatively spared. This work was supported by National Institutes of Health grant MH62103.

SENTENCE PROCESSING AND TEMPORAL LOBE FUNCTION IN SCHIZOPHRENIA: A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

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Deficits in language processing are a major symptom of schizophrenia. Previous research with functional imaging has shown attenuated brain activation during language comprehension in left fronto-temporal regions in schizophrenia, however studies have mainly focussed on processing of single words. We investigated brain activation with functional magnetic resonance imaging while subjects read sentences with congruent or incongruent semantic meaning. 30

short German sentence pairs, constructed de novo, served as stimuli. They were matched for length, tense and word frequency, and had either a congruent (e.g. "Das Klavier ist ein Musikinstrument? [the piano is a musical instrument]) or incongruent ("Das Klavier ist eine Tomate [the piano is a tomato]) meaning. Each sentence was presented for 5s with a 3s interstimulus interval. Groups of patients with DSM IV criteria of schizophrenia and healthy control subjects read sentences silently and judged by pressing one of two buttons whether the sentence was semantically correct in meaning. Data was collected from the whole brain (22 slices, slice thickness 5mm, TR=2s, TE=40 ms) using a 1.5 T Siemens SONATA system. All image processing and statistical analysis was performed using SPM99. Differential contrast for congruent vs. incongruent sentences was calculated for each subject. For the group statistics, a random effects model was used. Differential contrast for congruent > incongruent meaning showed robust activation in the left temporal pole, left hemisphere angular gyrus, anterior and posterior cingulate in healthy control subjects. Preliminary results suggest attenuated activation in patients with schizophrenia. The lateral temporal lobe is critically involved in assessing the overall sentence meaning in healthy subjects. Dysfunction of this brain region might contribute to language comprehension difficulties on a sentence level in schizophrenia.

ANALYSIS OF FMRI BOLD ACTIVATION DURING THE TOWER OF LONDON TASK USING CORTICAL PATTERN MATCHING

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We tested the hypothesis that novel cortical surface modeling approaches can permit more accurate localisation of functional deficits in schizophrenia, and more sharply defined activation foci. We created two average models of cerebral cortex from 3D structural magnetic resonance images (sMRI) of ten first-episode male patients with schizophrenia and ten age- and sex- matched controls. 3D functional magnetic resonance imaging (fMRI) BOLD activation data, obtained while subjects performed the 'Tower of London' task, was then mapped to both cortex models for comparison across diagnostic groups (patient and control) and between cortical alignment methods. The first average cortical model of cortex was created by identifying 17 sulci on each hemisphere of each subject's brain. These sulci were geometrically averaged, and each subject's cortex warped into alignment with the average sulci. The second average cortical model of cortex was developed by aligning individual sMRIs to a template, intensity averaging, and extracting the cortex from the resulting average image. fMRI data showed increased activation with task difficulty in the control group in the left Brodmann's areas 44, 7, 37, and 18 and in the right Brodmann's area 7. In the patient group, increased activation with task difficulty was seen in the left Brodmann's area 10 and in the right Brodmann's area 18. Significantly decreased activation with task difficulty was found in the left and right Brodmann's area 9 of the patient group; this was not observed in the control group. Sulcal averaging and cortical data warping resulted in sharper localisation of the functional data when compared to the functional data mapped to the cortical model derived from an average intensity brain. Future comparisons will relate these functional differences to differences in cortical grey matter density in patients and controls.

MODIFIED CEREBRAL ORGANIZATION FOR LANGUAGE IN SCHIZOPHRENIA: A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

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Aim : Several anatomical and functional imaging studies support the hypothesis that schizophrenia is a failure of hemispheric dominance for language (Crow, 1997). We investigated this theory by searching for differences in schizophrenic patients as compared to controls, hypothesing that patients had less marked left hemispheric asymmetry than controls during speech processing. Methods : 7 pairs of schizophrenic and healthy subjects, all right-handed, matched on sex, age and education levels were submitted to both 3D high resolution T1 and BOLD acquisitions (1.5-T GE Signa). Based on a previous study in our group (Mazoyer et al., 1993), we used a block design alternating eight 30-s duration periods of either auditory French (4 blocks) or Tamil (4 blocks) stories. Comprehension scores of the French story were obtained in each subject after fMRI completion. A group comparison of the French-Tamil contrast was performed (SPM99). However, comprehension scores differed between groups. In order to understand wether the group difference could be explained solely by comprehension scores, we performed a simple regression analysis of the same contrast using subject performances as a regressor over all subjects. Results : Group comparison evidenced a decrease of activation in schizophrenic patients in the following areas : left precuneus, median frontal gyrus, angular gyrus and superior temporal sulcus. In the three latter regions, the origin of such difference was in part explained by the story comprehension scores, as shown by the regression analysis. In the same vein, regions that were more activated in patients than in controls (right median frontal gyrus, precuneus and inferior parietal gyrus) were negatively correlated with the comprehension scores. Conclusion : Schizophrenic patients lower performances in speech processing went along with both lower left and larger right hemisphere regional activations. This reduced functional asymmetry supports in part the hypothesis of a lower hemispheric specialization for language in schizophrenia.

MOTOR CORTEX FMRI ACTIVATION CHANGES IN SCHIZOPHRENIA

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Impaired motor coordination is common in schizophrenic patients. It has been shown that patients are delayed in initiating movements, have prolonged reaction time, and carry out repetitive movements slowly. Previous fMRI studies which have examined motor function in schizophrenia suggest that there are motor system abnormalities in schizophrenia. However, the findings remain inconsistent and the functional correlates remain unclear. The purpose of this study was to ascertain whether activation differences could be identified in stable schizophrenic patients on the basis of BOLD measures in two motor regions, the primary motor cortex, Brodmann area 4 (BA4) and the premotor and supplementary motor area, Brodmann area 6 (BA6). Twenty two schizophrenic patients and 22 healthy control subjects were included in the study. Functional imaging was performed with a 1.5-T GE MRI scanner using gradient echo imaging during the completion of both a right and left sequential finger oppo-