

16. A Functional Imaging Study of Memory Impairment in Schizophrenia

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We examined brain activity in two groups of schizophrenic subjects, one with memory impairment and the other without. All subjects underwent 12 positron emission tomography (PET) scans while engaged in the encoding and recall of word lists. Memory load was manipulated by parametrically varying the length of the lists across scans. Comparisons with a group of age-matched, healthy controls showed a relative failure of left prefrontal activation and of bilateral temporal deactivations in both groups of schizophrenic subjects. Restriction of analyses to those scans in which performance was comparable across groups showed quantitatively normal prefrontal activity in the subjects with schizophrenia. Our results indicate both an abnormality of fronto-temporal interactions in schizophrenia and an abnormality in prefrontal function, the latter relating to memory performance.

Rationale

Schizophrenia is a chronic, deteriorating disorder characterized by, among other things, delusions, hallucinations, social withdrawal, and a number of cognitive deficits. Recent studies have shown that memory impairment can be a major feature, disproportionately exceeding other cognitive abnormalities. The memory impairment tends to be specific to episodic long-term memory and it has been shown that it is not explicable purely in terms of accompanying symptoms such as hallucinations.

Our previous work has suggested that the functional neuroanatomical abnormalities in schizophrenia may be conceptualized as a reversal of the normal interactions between the prefrontal and temporal cortex. Other studies have suggested that the core pathology in schizophrenia lies in a functional abnormality of the prefrontal cortex. Since PET studies of healthy volunteers performing long-term memory tasks have produced data which emphasizes the role of prefrontal cortex in memory, it seems likely that memory provides a useful arena in which to study the functional neuroanatomy of schizophrenia. We therefore used positron emission tomography (PET) to examine changes in brain activity related to the encoding and paced retrieval of word lists in groups of healthy control subjects and in patients with schizophrenia. Memory load was systematically manipulated by parametrically varying word-list length.

Subjects

Twelve subjects with schizophrenia (DSM III-R diagnosis), all on medication, and 6 healthy, age-matched control subjects were scanned. The subjects with schizophrenia were subdivided into two equal groups: Those showing memory impairment and those with preserved memory function.

Method

All subjects underwent 12 PET measurement of regional cerebral blood flow (rCBF) over a 2-hr period. During each PET scan they were engaged in the encoding and paced recall of word lists. Material was presented verbally at a rate of one word per 2 sec. On the completion of the list, subjects were required to retrieve as many items as possible, recall being paced by the experimenter. On completion of the retrieval stage, the list was read and recalled once more; this was repeated throughout scanning. Word list length varied across the 12 scans from 2 to 13 items inclusive.

Statistical parametric mapping (SPM) was used to analyze PET scan data. Scans were realigned and spatially normalized before a correction for changes in global blood flow and pairwise comparisons on a voxel by voxel basis. Data were analyzed for the main effects of memory load (i.e., which brain regions showed increases and decreases in activity in association with varying memory load). In addition, we examined the group-by-task interaction for regions where the subjects with schizophrenia showed significant failures in activation and deactivation in association with the memory task and for regions where brain activation was associated with the presence of memory impairment. A further stage of the analysis assessed activations in light of the degree to which subjects were successful in retrieving material.

Results

Memory-related activations and deactivations in control subjects. The control group showed activations in left lateral prefrontal cortex (PFC) and parietal cortex bilaterally. Deactivations were seen in superior temporal cortex bilaterally and in medial PFC. Analysis of data from subjects with schizophrenia showed a qualitatively similar pattern of activations and deactivations.

Group-task interactions. While showing a qualitatively similar pattern to control subjects, both groups of schizophrenic subjects showed significantly less left PFC activation and temporal deactivation. In addition, the group with impaired memory function showed a significant failure of parietal activation bilaterally. Direct comparison of the two groups of schizophrenic subjects showed a relative failure of parietal activation and of temporal deactivation in the memory-impaired group.

Relation to performance. Across those scans where performance in the schizophrenic subjects was comparable to controls, a normal degree of left PFC activation was observed while failure of temporal deactivation remained significant. In the group with impaired memory, bilateral parietal cortex continued to show an impaired activation.

Discussion

In brief, our study has shown patterns of abnormality in memory-related activity in schizophrenia. First, left PFC activations were significantly less than in control subjects and this can, perhaps, be interpreted as a failure to apply appropriate encoding strategies. The finding that left PFC activation in schizophrenic subjects was statistically indistinguishable from control subjects when effects of impaired performance were removed is an interesting one indicating, as it does, that it is not an inability to activate PFC per se which lies at the core of the abnormality. Rather, it seems that, when the demands of the task become excessive, there is a falling off of normal activity and this is associated with a failure to optimally encode information. The second abnormality, that of a failure of temporal cortex deactivation has been conceptualized as an abnormality of the normal pattern of fronto-temporal integration. This abnormality was not affected by performance and might conceivably indicate a core pathology in schizophrenia.