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**Genetic and Environmental Influences On Brain Function in Schizophrenia. an FMRI Study of the Maudsley Twin and Family Cohorts.**

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**Introduction:** The heritability of the brain's structure and function in schizophrenia remains elusive

**Objectives/Aims:** To assess the influence of genetic and environmental factors on executive function in schizophrenia.

**Method:** A twin-sibling study of 206 subjects; 163 twins, varying in their zygosity and concordance for schizophrenia, and 43 singletons from sibling clusters varying in their concordance for schizophrenia. We assessed performance and regional brain activation using functional magnetic resonance imaging, during a phonological verbal fluency task.

**Results:** Patients and their unaffected relatives developed greater activation in the left inferior frontal gyrus, and greater deactivation in the middle temporal gyri bilaterally. These features were maximally evident in subjects with schizophrenia. When the analysis was restricted to the unaffected relatives and healthy controls, a similar pattern was evident. Heritability was greatest in the left hippocampus and the right middle temporal gyrus. Genetic modelling indicated a phenotypic correlation between schizophrenia and increased activity in the inferior frontal gyrus and reduced activity in the left middle temporal gyrus and left hippocampus, which appeared principally due to shared genetic effects.

**Conclusions:** Both schizophrenia and its familial vulnerability were associated with altered frontal, parahippocampal and temporal activation during verbal fluency. The altered left inferior frontal activity was particularly associated with schizophrenia, while altered left medial temporal and right middle temporal activity were more heritable. The latter was more intimately linked to the genetic risk for schizophrenia, and thus the better candidate intermediate phenotype.