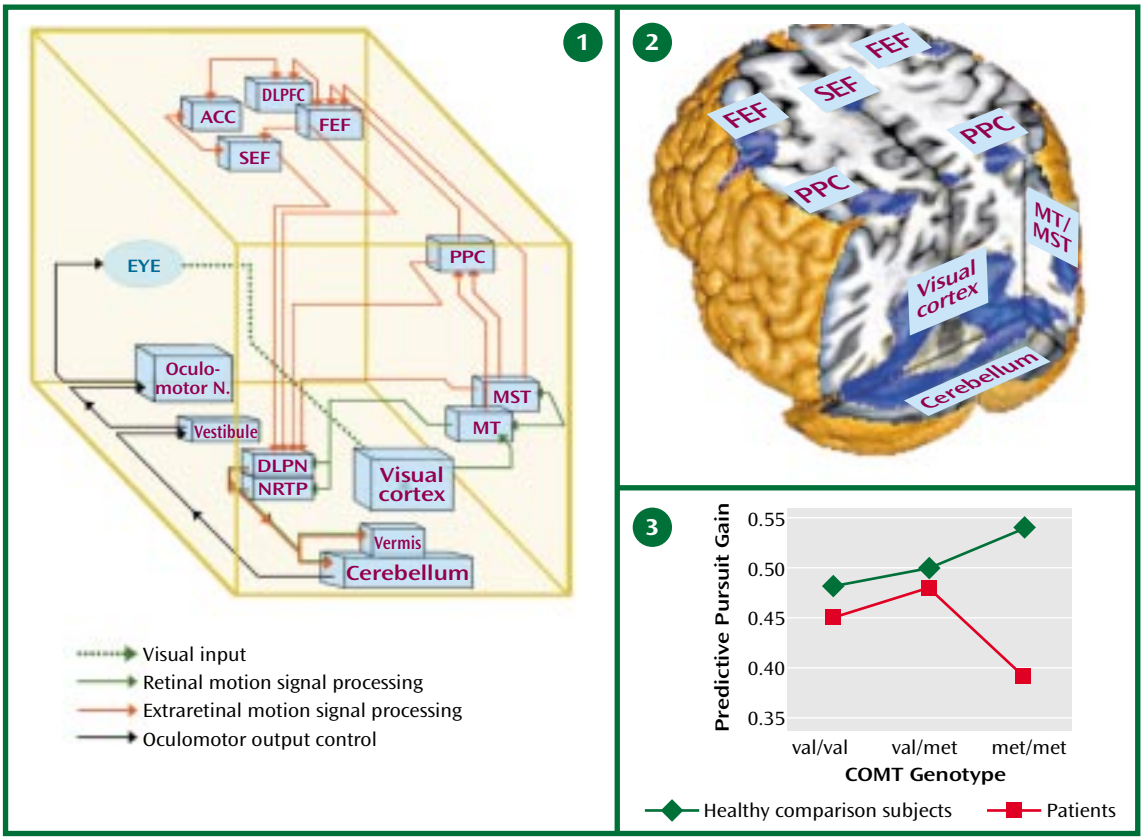
Carol A. Tamminga, M.D., Editor

Schizophrenia, VII



ACC: anterior cingulate cortex; DLPFC: dorsolateral prefrontal cortex; DLPN: dorsolateral pontine nucleus; FEF: frontal eye field; MST: medial superior temporal lobe; MT: middle temporal lobe; NRTP: nucleus reticularis tegmenti pontis; PPC: posterior parietal cortex; SEF: supplemental eye field.

Defining the Neurobiology of Risk Factors

Distinct behavioral and neural characteristics are likely to be associated with risk for schizophrenia. Abnormal smooth pursuit eye movements are a good phenotype candidate because they are one of the most consistently observed biological changes associated with genetic risk for the illness. Much of the neural circuitry responsible for smooth pursuit eye movements in human and nonhuman primates has been described and is depicted in part 1 of the figure. One of the main deficits in smooth pursuit eye movements in schizophrenia is a tendency for the velocity of the patient's eyes to lag behind the velocity of a moving object. Two components contribute to this response: 1) retinal guided motion, or the use of immediate motion information of the image on the retina to change eye movements (green line), and 2) extraretinal guided motion, or the use of previous target and eye motion information to change subsequent eye motion (red line). The two neural pathways in the brain mediating these motions only partly overlap. Persons with schizophrenia and their biological relatives perform smooth pursuit eye tracking abnormally under predictive pursuit conditions; this suggests an abnormality in extraretinal motion processing. To identify the cerebral regions responsible for an abnormality in extraretinal motion processing, we used functional magnetic resonance imaging during a pursuit task. Persons with schizophrenia performed the overall task similarly to healthy comparison subjects but showed alterations in their predictive pursuit. Contrasting the pursuit-related brain activations in the schizophrenia and the comparison groups, we found decreases in the blood oxygenation level-dependent activations in the frontal eye field, supplemental eye field, and medial superior temporal lobe in the schizophrenia patients (Figure, part 2), all areas previously identified in nonhuman primates as associated with extraretinal motion processing. These data made clearer the mechanisms of schizophrenia risk factors and how these risk factors affect cerebral processing. This also demonstrates that it is increasingly informative to examine the association of specific risk factors, the related distinct genotypes, and the neural correlates. Indeed, we observed an interesting relationship between the COMT genotype and predictive pursuit in which the COMT alleles associated with enhanced prefrontal functioning are paradoxically associated with poor predictive pursuit (Figure, part 3).

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