COMT GENOTYPE IN SCHIZOPHRENIA:
COGNITIVE PERFORMANCE AND BRAIN
CIRCUITS

Dopamine levels in the prefrontal cortex seem to play a crucial role in cognitive functioning in schizophrenia. The functional polymorphism of the COMT (catechol-o-methyltransferase) enzyme could mediate the relationship between dopamine levels, cognitive functioning and neural activity of the prefrontal cortex (1). The val allele results in a high functioning enzyme which degrades dopamine from the synapsis more rapidly than the low functioning enzyme (met allele). The val/val polymorphism should be associated with less dopamine in the prefrontal cortex and therefore with poorer cognitive performance and dysfunctional brain activity in the prefrontal cortex than the met/met polymorphism. Context processing deficits have been shown to be specifically present in schizophrenia and linked to hypofrontality (2). This specific measure of executive functioning should be more related to genetic variations than more general cognitive deficits (3).

GOALS:
1. To investigate the impact of the val158met COMT polymorphism on several neuropsychological and cognitive domains in schizophrenia.
2. To study the impact of the val158met COMT polymorphism on prefrontal cortical function in schizophrenia during context processing tasks.

METHODS
Neuropsychological testing:
MATRICS battery
We studied a sample of 68 schizophrenia spectrum disorder patients. Subjects performed several tests of the MATRICS Consensus Cognitive Battery to measure the performance in the cognitive domains of speed of processing, working memory, verbal learning and visual learning.
Genotyping for COMT val158met polymorphism was accomplished by PCR-RFLP analysis.

Cognitive testing:
DPX Task
36 schizophrenia spectrum disorder patients performed the Dot version of the expectancy AX continuous performance task (DPX task).

Functional Imaging:
fMRI

RESULTS
MATRICS BATTERY

DPX TASK

fMRI

CONCLUSIONS
Our results show that the COMT genotype impacts in the neuropsychological and cognitive performance of schizophrenia spectrum patients probably through dopamine availability in the prefrontal cortex. Prefrontal brain activity of context processing deficits in schizophrenia may be mediated by COMT genotype effects. COMT genotype may be relevant to schizophrenia treatment through its involvement in dopamine metabolism.

REFERENCES

AUTHORS DISCLOSURE NO POTENTIAL CONFLICT OF INTEREST