M53. GENE EXPRESSION ALTERATIONS RELATED TO MANIA AND PSYCHOTIC SYMPTOMS IN PERIPHERAL BLOOD OF PATIENTS WITH A FIRST EPISODE OF PSYCHOSIS

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Background Psychotic disorders, such as schizophrenia and bipolar disorder, affect approximately 3% of the general population. The symptoms include hallucinations, delusional beliefs, severe mood variations, and cognitive impairment. However, these clinical aspects may be difficult to distinguish from one another, mainly during the early stages of psychosis. The first-episode psychosis (FEP) is a critical period given that brain abnormalities and cognitive deficits are already present and progress faster and more aggressively in the first years of the disorder. We investigated differences in the mRNA levels of 12 genes among individuals with FEP of schizophrenia spectrum disorder (FEP-S; N=53), FEP with mania (FEP-M; N=16), and healthy controls (N=73). We also verified whether gene expression is correlated to clinical features, including functional impairment and severity of psychotic, manic, and depressive symptoms. The study aims are to differentiate FEP-M and FEP-S, improving early diagnosis and adequate intervention.
Methods Antipsychotic-naïve FEP patients (N = 69) were recruited from a psychiatric emergency unit in São Paulo, Brazil. Trained psychiatrists established the diagnosis of a psychotic disorder and patients were assessed at baseline and followed up for at least two months. At the end of follow-up, patients with a schizophrenia or schizophreniform disorder diagnosis were classified as FEP-S (N = 53) and patients who met bipolar disorder (with psychotic symptoms) diagnostic criteria were classified as FEP-M (N = 16). Healthy controls were age- and gender-matched with no current or previous diagnosis of a psychiatric disease or family history of a psychotic disorder (N = 73). A total of 5 mL of whole blood was collected in PAXgene® RNA tubes and RNA was isolated with PAXgene Blood RNA kit. Approximately 400 ng of each RNA sample was reverse-transcribed. The expression of 12 psychotic-disorder-related genes was evaluated by quantitative PCR. Gene expression was quantified using the relative threshold method (Crt) with the geometric mean (GM) between ACTB and GAPDH as the endogenous control.
Results AKT1 and DICER1 expression levels were higher in FEP-M patients compared to that in FEP-S patients and healthy controls, suggesting that expression of these genes is associated more specifically to manic features. DICER1 expression was positively correlated to the PANSS (positive and negative syndrome scale) excitement dimension and YMRS (young mania rating scale) total score. Furthermore, MBP and NDEL1 expression levels were higher in FEP-S and FEP-M patients than in healthy controls, indicating that these genes are psychosis-related (independent of diagnosis).
Discussion To our knowledge, this is the first study that compares gene expression in antipsychotic-naïve FEP-M and FEP-S, suggesting potential diagnostic specificities. Based on an integrated model, we propose that MBP and NDEL1 are upregulated in FEP-S and FEP-M patients, who all exhibit psychotic symptoms. Moreover, two other genes, AKT1 and DICER1, were upregulated in FEP-M patients only, indicating that these genes could be related to mania, independently of psychotic symptoms. Although further validation is needed, our findings suggest that genes related to

neuronal development are altered in psychotic disorders, and some of them might support the differential diagnosis between schizophrenia and bipolar disorder in the near future, which in turn could have an impact on the treatment of these disorders.
Disclosure: Nothing to Disclose.