Article: EPA-1035
Topic: EPW26 - Bipolar Disorders 1

THE ANK3 RISK GENE FOR BIPOLAR DISORDER MODULATES BRAIN REGIONAL ACTIVITY DURING A WORKING MEMORY TASK

G. Delvecchio[1], D. Dima[1], S. Frangou[2]

[1]Social Genetic & Developmental Psychiatry (SGDP) (PO80), Institute of Psychiatry, London, United Kingdom ; [2]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, USA

Introduction: Genome-wide association studies indicate that two single-nucleotide polymorphisms (SNPs) in the ANK3 gene, rs10994336 and rs9804190, increase the risk for bipolar disorder (BD). The ANK3 gene encodes the ankyrin-G protein and influences neuronal firing by changing sodium channel functions, thus impacting on brain regional activation.

Objectives: We examined the effect of the two ANK3 SNPs on brain activation during a working memory task.

Aims: The aim of our study is to investigate whether the genetic risk associated with the two SNPs is coupled with abnormal activation in the working memory network.

Methods: We used functional magnetic resonance imaging data to investigate the impact of ANK3 rs10994336 and ANK3 rs9804190, on brain activity during a 3-back working memory task in 41 BD patients, 25 unaffected first-degree relatives and 46 healthy individuals (HI).

Results: For the ANK3 rs10994336 (risk allele T), significant diagnosis x genotype interactions were observed in the left prefrontal (BA10/BA11), anterior cingulate (BA32/BA25) and posterior cingulate (BA31) cortex. These regions, risk allele carriers who were either patients or unaffected relatives showed increased activation compared to healthy controls carrying the risk allele. For the ANK3 rs9804190 (risk allele C) a significant effect of genotype was found in the right anterior cingulate (BA24), where subjects carrying the risk allele showed decreased activation compared to subjects carrying the protective allele.

Conclusions: Our data demonstrate that the effect of ANK3 rs10994336 and ANK3 rs9804190 on the brain converges on key regions involved in working memory processing.

https://doi.org/10.1016/S0924-9338(14)78325-7 Published online by Cambridge University Press