GENETIC VARIABILITY AT IMPA2, INPP1 AND GSK-3β INCREASES THE RISK OF SUICIDAL BEHAVIOUR IN BIPOLAR PATIENTS


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INTRODUCTION

Among other psychiatric illnesses, Bipolar disorder (BD) presents the highest rates of suicidality1. Lithium, one of the most widely used mood stabilizers in BD, has been reported to present antidepressive properties2. Although its mechanism of action has not been fully elucidated, there is further insight regarding the implication of both the Phosphoinositol and the Wnt/β-catenine pathways in it3.

OBJECTIVES

Our goal was to verify whether molecular variation at IMPA2, INPP1 and GSK-3α and GSK-3β genes could be considered as potential genetic markers for suicide behaviour (SB) in BP.

METHODS

199 unrelated Caucasian bipolar type I or II outpatients (102 males and 97 females) were recruited from the Bipolar Disorder Unit of the Hospital Clinic of Barcelona and from primary care settings from Oviedo. All patients were grouped and compared according to the presence or the absence of history of SB (defined as the presence of at least one suicide attempt). Genomic DNA was extracted from blood samples from each participant, according to standard protocols. Several polymorphisms at the IMPA1, IMPA2, INPP1, GSK3α and GSK3β genes were genotyped.

RESULTS

Single marker analysis revealed several associations between some of the variants at the IMPA2, INPP and GSK-3β genes and SB in our BP sample, on both genotypic and allelic level (Table 1 and 2). No association was detected between the IMPA1 and GSK-3α gene polymorphisms and SB.

Patients carrying AA and GG genotypes of the rs669838-IMPA2 gene and the rs4853694-INPP1 gene, respectively, presented higher risk of committing a SA. Concerning the GSK-3β gene, two SNPs were found to be associated with the emergence of SB.

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CONCLUSIONS

Our results suggest that genetic variability at IMPA2, INPP1 and GSK3β is associated with the emergence of SB in BP. Therefore our data would strengthen those studies which have suggested the potential significant role of genetic variability at the phosphoinositol signaling pathway and the Wnt/β-catenine pathway in both suicide and bipolar disorder.

REFERENCES


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