LITHIUM RESPONSE: ASSOCIATION STUDY WITH CANDIDATE GENES

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Following the introduction of lithium in the treatment of bipolar disorder, numerous studies have addressed its mechanism of action, and particularly its role in the aminergic neurotransmission. Lithium is not effective in all bipolar patients. Differences in lithium response might be attributable to the genes putatively involved in lithium's mechanism of action. The aim of our study is to investigate the role of the genetic variants influencing the response to mood stabilizing therapy with lithium. We studied some candidate genes such as those of receptors and transporters of dopaminergic and serotonergic systems and the gene of inositol polyphosphate 1-phosphatase, the latter implied in the mechanism of action of lithium. We genotyped a sample of 66 patients affected by bipolar disorder and 106 healthy Sardinian anonymous blood donors as controls. Bipolar patients were recruited at the outpatients unit of our Section. Lifetime consensus diagnoses according to RDC criteria were achieved by trained clinical psychopharmacologists using data from a personal semi-structured interview and a systematic review of patients' medical records. The life-chart method was used to evaluate the effectiveness of lithium prophylaxis: mood fluctuations were scored independently by the clinical research staff and plotted on a time line. Response to lithium therapy was evaluated applying the *retrospective evaluation of prophylactic treatment response scale* to the life-chart data: responders were defined as patients who had a total score of 7 or higher. We found 48 responders and 18 non responders. The local Ethical Committee approved the study and informed written consent to participate in the study was obtained from all patients. Genomic DNA was extracted from whole blood by NaCl precipitation. SNP analysis was performed by PCR/RFLP or an ABI Prism 7900HT instrument using Assays-On-Demand reagents from Applied Biosystems, Inc. Allele and genotype frequencies of responders and non responders were compared by means of Chi-Square analysis or Fisher's exact test. We did not find any statistically significant difference in allele and genotype frequencies between responders and non responders. All polymorphisms were in Hardy Weinberg Equilibrium in responders, non responders and controls. As for allele frequency, allele 1 of 5-HTTRL was over-represented in non responders compared to controls ($p=0.048$). Our preliminary analysis does not show any significant difference in these candidate genes between responders and non responders. We are currently genotyping a larger sample in order to increase the statistical power and find a possible association between lithium response and these candidate genes.