SEARCHING SINGLE NUCLEOTIDE VARIATIONS RELATED TO NEUROLEPTIC MALIGNANT SYNDROME SUSCEPTIBILITY

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Introduction: Neuroleptic Malignant Syndrome (NMS) is a rare and potentially life-threatening adverse reaction associated with administration of antipsychotic or other central dopamine (D2) receptor antagonists, and characterized by hyperthermia, muscular rigidity, altered consciousness, variable blood pressure, sweating and accelerated heart rate. Cases of NMS triggered by antidepressants, lithium, sudden withdrawal of dopaminergic drugs and substance abuse, such as amphetamine, have also been reported. Depending on antipsychotics health treatments, a 0.02-3% range of patients may develop the NMS, among which about 10-20% has a fatal outcome. Although the occurrence of NMS is typically unpredictable, high environmental temperature, dehydration, concurrent medical conditions, polypharmacy, initial treatment or dosage changes have been considered risk factors that can trigger the onset of this syndrome. Case reports of familial occurrence have also been described suggesting a putative genetic background for susceptibility to NMS. So far, a limited number of polymorphisms associated with few genes have been investigated, however no genetic biomarkers for NMS predisposition have been clearly identified.

Material and methods: A cohort of NMS patients and healthy subjects have been enrolled for single nucleotide variations (SNVs) analysis of the dopamine D_2receptor gene. Genomic DNA was extracted from peripheral venous blood by standard techniques, amplified by polymerase chain reaction and sequenced.

Results: So far, we have found a frequency of the analyzed SNVs of the control cohort that is comparable to the frequency of the European population along the coding and the regulatory regions of the DRD2gene. On the contrary, an increased frequency of a SNV mapped in the regulatory region of the DRD2gene have been detected in the cohort of the NMS patients.

Discussion and conclusions: D2receptor plays a major role in the central dopaminergic activity in thermoregulation, motor coordination and muscle tone. Although preliminary, our results suggest that genetic variations of the DRD2promoter may influence the transcription levels of the gene that could result in a modified D2receptor activity.