Etiology of bipolar disorder

Etiology of Bipolar Disorder The bipolar psychiatric disorder, as the suggests, is an illness in which the sufferer fluctuates between depression and mania. According to the latest figures it affects 5. 7 million Americans presently and its existence in rest of the world is well recognized (Duckworth, 2007). It has assumed such serious proportions in the present human population that the World Health Organization (WHO) has categorized as the 6th leading cause of disability worldwide (Gould et al, 2004). Initial therapeutic interventions tried for the disorder were mainly pharmacological but lately intensive psychotherapy is being increasingly recognized as a better alternative, although absolute therapy is still considered to be in its experimental stages. There have numerous studies to explain the etiology of the disease which have progressed from explanations of behavioral, social and psychological factors as its causes to the imbalance of neurotransmitters in the brain and genetic defects making certain individuals particularly prone to it.

As bipolar psychiatric disorder is characterized by sporadic, alternating events of depression and hyper manic state, the excitatory and inhibitory neuronal transmission have been the prime targets of pharmacological interventions. Molecular and cellular targets include inhibition of enzymes such as inositol monophosphatase, inositol polyphosphate 1-phosphatase, etc. by the administration of lithium salts whereby the lithium ion competes for a magnesium binding site which is responsible for prompting the action of such enzymes (Gould et al, 2004). Similarly valproate and carbamazapine inhibit another set of enzymes, as well as molecular signaling pathways in neuronal transmission. Inhibition of these enzymes is responsible for the tentative therapeutic action.

Another aspect which has been noticed in psychiatric disease is the high

heritability of schizophrenia as well as bipolar disorders which points a finger at the genetic predisposition to such disorders (Owen et al, 2004).

Experimental studies in molecular genetics are already underway and chromosomal abnormalities have been noticed at specific locations of the human genome obtained from sufferers of psycho somatic disease. In bipolar disease, involvement of multiple genes has been suspected for long and studies are therefore intricate in design, but feasible with the modern tools of molecular biology which have become available only recently. In a genome wide association study conducted on pooled samples obtained primarily from European patients, genotyping of over 550000 single nucleotide polymorphisms revealed that the strongest association signal was detectable at a marker within the first intron of diacylglycerol kinase eta (Baum et al, 2008). The specific gene encodes DGKH, a key protein in lithium sensitive phosphatidyl inositol pathway (Baum et al, 2008). This led the authors to infer that bipolar disorder is a reproducible polygenic disease.

Another study carried out on samples obtained from patients belonging to a particular Scottish genetic pool, with care to include only persons from large extended families, the genome scan revealed that psychiatric disease susceptibility, particularly schizophrenia and bipolar disorder were linked to the 1q42 region of the genome (Macgregor et al, 2004). Another experimental study found a linkage for bipolar disorder on chromosome 8q24 and the authors suggested the putative candidate genes as thyroglobulin, KCNQ3 coding for a volatge gated potassium channel and the gene for adenyl-cyclase (Avramopoulos et al, 2004).

Current evidence of a genetic link for Bipolar disorder as well as other psychiatric diseases like schizophrenia and obsessive compulsive disorders is

therefore is gradually emerging and the need for identification of the genomic regions responsible for the susceptibility to such disorders is therefore the focus of future research in this field. The results obtained until now are inconsistent with many regions in the human genome being identified as putative loci for susceptibility and further research is needed to fine tune the exact locus in order to develop better therapeutic approaches.

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