IMMUNE SYSTEM RELATED METABOLIC AND GENETIC ASPECTS IN DEPRESSIVE DISORDERS

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Background: The involvement of immune mechanism in psychiatric disorders was proposed in macrophage theories of depression and schizophrenia. Later, the involvement of the inflammatory related changes beyond the cytokines including the interaction between inflammatory response system and neuroactive tryptophan metabolites that brought imbalance in neuroprotective kynurenic acid arm and neurodegenerative 3-hydroxykynurenine and quinolinic acid arm of the tryptophan catabolic pathway was proposed in neuro-degeneration hypothesis of depression.

Method: A series of studies on human plasma and CSF changes and their associations to clinical symptoms and response to treatment and certain SNPs of genes from the related enzymes were carried out.

Results: It was observed that the neuroprotective, kynurenic acid was significantly lower and one of the neurodegenerative metabolites 3-hydroxykynurenine was higher in the plasma of drug naïve depressed patients. The plasma kynurenic acid concentration and neuroprotective ratio (kynurenic acid/kynurenine) gave clear discrimination between the patients and controls with reasonable sensitivity and the specificity. The CSF findings showed similar direction. The findings were also supported by the findings from SNPs polymorphism of kynurenine amonitransferase III enzyme which indicated the significant association with a haplotype and depressive symptoms in combination with anxiety in both unipolar and bipolar depression.

Conclusion: The major depressive disorder is associated with imbalanced immune-metabolic-neurochemical systems.