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Poster Presentation

The Role of Kynurenine Pathway in Suicidal Behavior and Depression

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Abstract

According to global statistics, over 80,000 deaths occur by suicide annually. Up to 90% of complete suicides are based on psychiatric disorders specifically major depressive disorder (MDD) and bipolar disorder. Furthermore high levels of inflammation have been indicated in suicidal patients in both central nervous system and the peripheral blood. Two biological mechanisms that play a key role in suicidal behavior and ideation are: 1-presenting cytokine receptors on neurons in specific area, 2- Activation of kynurenine pathway of tryptophan catabolism. The kynurenine pathway is started by the conversion of tryptophan (TRP) to N-formylkynurenine. This conversion is occurred by any of these enzymes: indoleamine 2,3- dioxygenase 1 (IDO1), IDO2, or tryptophan 2,3-dioxygenase (TDO). The resulting N-formylkynurenine is converted to kynurenine (KYN), which is a precursor of bioactive compounds, such as quinolinic acid (QUIN), kynurenic acid (KYNA), picolinic acid (PIC), and 3-hydroxyanthranilic acid (3-HAA). The first evidences about the relationship between the dysregulation of the kynurenine pathway and suicidal behavior was reported in 2011. A high level of kynurenine in plasma was detected in suicidal attempters with depression compared to non-suicidal depressed patients. Based on recent study the levels of tryptophan in plasma was 40% decreased and KYN/TRP was 40% increase in suicidal adolescent with MDD, compared to non-suicidal individuals with MDD and healthy controls. Imbalance of neuroactive metabolites is a result of association between inflammation and dysregulation of kynurenine pathway in suicidal patients. Furthermore levels of kynurenine metabolites and inflammatory cytokines are increased in the cerebrospinal fluid of suicidal patients. Therefor any aberration in this pathway causes a specific pathogenic mechanism linking inflammation and suicidal/depressive symptoms.

Keywords: Neuroinflammation, Suicide, Depression, Kynurenine

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