Article: 1302
Topic: EPV08 - e-Poster 08: Depression

Differenital Behavioral and Neural Consequences of Serotonin and Catecholamine Deficiency in Depression: an Experimental Study

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Introduction: Psychopathological and biological markers that predict response to antidepressant drugs that selectively increase serotonin and/or chatecholaminergic neurotransmission will considerably increase the effects of currently available treatment options.

Objectives: Comparison of tryptophan depletion (TD) and catecholamine depletion (CD) regarding the pathogenesis of depressive symptoms.

Aims: To elucidate the differential symptomatology and neurocircuitry in response to reductions in serotonergic and catecholaminergic neurotransmission in subjects at high risk of depression.

Methods: Using identical neuroimaging procedures with [18F] fluorodeoxyglucose positron emission tomography after TD and CD, subjects with remitted depression were compared to healthy controls in a double-blind, randomized, crossover design.

Results: While TD induced significantly more depressed mood, sadness and hopelessness than CD, CD induced more inactivity, concentration difficulties, lassitude and somatic anxiety than TD.CD specifically increased glucose metabolism in the bilateral ventral striatum and decreased glucose metabolism in the bilateral orbitofrontal cortex, whereas TD led to a specific increase in glucose metabolism in the right prefrontal cortex and in the PCC. While we found direct associations between changes in brain metabolism and induced depressive symptoms following CD, the relationship between neural activity and symptoms was less clear after TD.

Conclusions: This study showed that serotonin and catecholamines play common and differential roles in the pathophysiology of depression. Thus, the development of psychopathological and neuronal markers predicting response to selective monoamine inhibition is feasible, and current efforts to develop antidepressants with dual and triple reuptake inhibition (serotonin, norepinephrine, dopamine) are supported by this study.

https://doi.org/10.1016/S0924-9338(15)31019-1 Published online by Cambridge University Press