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5-HTP HYPOTHESIS OF SCHIZOPHRENIA

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Introduction and aims: To pose a new hypothesis of schizophrenia that affirm and unifies conventional hypotheses.
Methods: Outside the brain, there are 5-HTP-containing argyrophil cells that contain tryptophan hydroxylase 1 without L-aromatic amino acid decarboxylase. Monoamine oxidase in the liver and lung metabolize 5-HT, rather than 5-HTP, and 5-HTP freely crosses the blood–brain barrier, converting to 5-HT in the brain. Therefore I postulate that hyperfunction of 5-HTP-containing argyrophil cells may be a cause of schizophrenia. I investigate the consistency of this hypothesis with other hypotheses using a deductive method.
Results: Overactive 5-HTP-containing argyrophil cells produce excess amounts of 5-HTP. Abundant 5-HTP increases 5-HT within the brain (linking to the 5-HT hypothesis), and leads to negative feedback of 5-HT synthesis at the rate-limiting step catalyzed by tryptophan hydroxylase 2. Due to this negative feedback, brain tryptophan is further metabolized via the kynurenine pathway. Increased kynurenic acid contributes to deficiencies of glutamate function and dopamine activity, known causes of schizophrenia.
Conclusions: The 5-HTP hypothesis affirms conventional hypotheses, as the metabolic condition caused by acceleration of tryptophan hydroxylase 1 and suppression of tryptophan hydroxylase 2, activates both 5-HT and kynurenic acid. In order to empirically test the theory, it will be useful to monitor serum 5-HTP and match it to different phases of schizophrenia. This hypothesis may signal a new era with schizophrenia treated as a brain-gut interaction.

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