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The role of the kynurenine metabolism in major depression

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Abstract There are circumferential evidences that major depression is associated with mild pro-inflammatory state. Both physiological and psychological stress can induce increased production of pro-inflammatory mediators, reactive oxygen species (ROS) and hypothalamo–hypophyseal–adrenal axis disturbances. While both pro-inflammatory mediators and ROS could activate the tryptophan breakdown and kynurenine pathway with a shift toward the neurotoxic arm, chronic hypercortisolism could also enhance tryptophan breakdown and induce neurodegenerative changes. The imbalanced kynurenine metabolism in terms of neuroprotective and neurotoxic effects was demonstrated in major depression, and in drug-induced neuropsychiatric side effects, such as interferon-treated depression. The changes in periphery are shown to be associated with central changes. Those changes might be partly contributed by genetic factors. While some of the currently available antidepressants could reverse the pro-inflammatory state of the depressed patients, these medications could not efficiently improve those metabolic and neurochemical changes within the period that could induce clinical improvement. In this review, the role of kynurenine metabolism which interacts with other neurochemicals is discussed as a major contributing pathophysiological mechanism in major depression. Moreover, the future therapeutic opportunities are also discussed in this review.