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The kynurenine pathway and the brain: challenges, controversies and promises

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Abstract

Research on the neurobiology of the kynurenine pathway has suffered years of relative obscurity because tryptophan degradation, and its involvement in both physiology and major brain diseases, was viewed almost exclusively through the lens of the well-established metabolite serotonin. With increasing recognition that kynurenine and its metabolites can affect and even control a variety of classic neurotransmitter systems directly and indirectly, interest is expanding rapidly. Moreover, kynurenine pathway metabolism itself is modulated in conditions such as infection and stress, which are known to induce major changes in wellbeing and behaviour, so that kynurenines may be instrumental in the *etiology* of psychiatric and neurological disorders. It is therefore likely that the near future will not only witness the discovery of additional physiological and pathological roles for brain kynurenines, but also ever-increasing interest in drug development based on these roles. In particular, targeting the kynurenine pathway with new specific agents may make it possible to *prevent* disease by appropriate pharmacological or genetic manipulations.

The following overview focuses on areas of kynurenine research which are either controversial, of major potential therapeutic interest, or just beginning to receive the degree of attention which will clarify their relevance to neurobiology and medicine. It also highlights technical issues so that investigators entering the field, and new research initiatives, are not misdirected by inappropriate experimental approaches or incorrect interpretations at this time of skyrocketing interest in the subject matter.

Keywords

3-Hydroxykynurenine, Kynurenic acid, Neuroimmunology, Neurology, Psychiatry, Quinolinic acid

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