Amino Acids (2000) 19: 1–2

Amino
Acids

Satellite on Neurobiology

General Introduction

The *6th International Congress on Amino acids, Bonn, Germany, August 3-7, 1999*, chaired by Dr O. Labudova and Professor H. Rink (Rheinische Friedrich-Wilhelms-Universität, Experimentelle Radiologie und Strahlenbiologie, Bonn) provided a framework for a *Satellite on Neurobiology*, a forum for discussing the issue of amino acids, which are essential components of metabolic pathways, required for the development and function of the central nervous system (CNS) (e.g. histidine, phenylalanine, tryptophan), but also precursors for the synthesis of several neurotransmitters (e.g. tyrosine, glutamine, arginine). Amino acids also play a role as neurotransmitters and/or neuromodulators (e.g. glutamate, aspartate, GABA, glycine), being present in specific neuronal pathways and acting upon release on specific receptors, whose structure, selectivity, transduction components, location and functions are presently beginning to be identified and further characterised. As neurotransmitters, amino acids may exert important functions, relevant for motor and integrative behaviour, but also promote functional and neurodegenerative deficits, via aberrant metabolic pathways leading to the production of free radicals, or via receptor-mediated overactivation leading to excitotoxicity. Thus, the characterisation of the neurochemistry of amino acids and of their receptors is a goal for understanding the pathophysiology of several disorders affecting the CNS, but also for discovering novel targets for pharmacological treatments aiming at a wide spectrum of clinical conditions.

In Chapter I, the authors discuss several experimental models for characterising neurocircuitries *in vitro* (including pathways releasing amino acids), and focusing on studies demonstrating the plasticity of the functional phenotypes. The studies propose models for bridging *in vivo* and *in vitro* experimental paradigms.

In Chapters II and III, the authors write about two important excitatory amino acid receptor families, the metabotropic and the ionotropic families. In Chapter II, the focus is on metabotropic receptors and on their involvement in anxiety, psychosis and Parkinson's disease, while in Chapter III, the focus is on NMDA receptors and on the original assumption that low affinity may constitute a desirable pharmacological feature.

In Chapter IV, the authors deal with the neuronal loops of the ventral basal ganglia, a region providing an example of how glutamate is interacting with dopamine for modulating the information flow required for integrative behaviour. An imbalance between glutamate and dopamine transmission may

be the pathophysiological substrate for neurodegenerative and functional disorders, such as Parkinson's disease and schizophrenia.

Excitatory amino acids may be involved in excitotoxicity and neurodegeneration, via direct overactivation of glutamate receptors or via a cascade of intracellular events involving poly(ADP-ribose)polymerase and transcription factors such as NF-kB and p53. This issue is discussed in Chapter V. The possibility that excitotoxicity can also be triggered by overactivation on voltage sensitive sodium channels or via the kynurenine pathway is also discussed. The kynurenine pathway of tryptophan degradation is thoroughly presented in Chapter VI, where it is proposed that, while quinolinic acid may induce excitotoxicity, kunureninic acid may be a neuroprotective factor.

That no single compound or factor can be made responsible for all the pathological mechanisms of cell injury is discussed in Chapter VII. The idea that endogenous neurodestructive and neuroprotective substances are simultaneously released during CNS insults, and that the balance among these factors will determine the final outcome is formulated. The authors propose new roles for heat shock proteins, nitric oxide and carbon monoxide, which should be considered when developing new therapeutic strategies for treating disorders affecting the CNS.

The *Satellite on Neurobiology* at the *6th International Congress on Amino Acids* gave the opportunity to present and discuss many new fascinating ideas on the role of amino acids in the CNS. Therefore, the editors would like to use this opportunity to acknowledge the fundamental support given by Merck KGaA, Darmstadt, Knoll AG Allgemeine Pharmakologie & ZNS Forschung, Ludwigshafen, Grünenthal GmbH, Aachen, Germany; Merck Sharp & Dohme Research Laboratories, Harlow Essex, UK; Novartis Pharma AG, Basel, Switzerland.

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