Reply: cannabinoid paths to anti-diarrheal drugs

We are delighted at this opportunity to discuss an important facet of the endogenous cannabinoid system, which we had overlooked more for the sake of space than for lack of interest. We agree with Capasso and his colleagues that the presence of cannabinoid receptors in the gastrointestinal tract is of considerable physiological and pharmacological relevance. As these authors point out, a substantial body of evidence indicates that cannabinoid drugs inhibit intestinal motility in rodents, presumably by targeting cannabinoid receptors in the gastrointestinal tract. This view is supported by the recent work of Capasso et al. (1999) in which they demonstrated that cannabinoid agonists inhibit intestinal motility in mice.

In astrocyte–neurone crosstalk: variants of the same language?

In a TiPS recent article1, Gallo and Ghiani review much of the most recent data on the expression of different glutamate receptors in glial cells. In addition, the authors provide an excellent survey of the current understanding of the regulation and function of these receptors in glia. By summarizing the available data on glutamate–receptor–mediated neurone–glia interactions, the authors emphasize the emerging view that a close bidirectional communication between neurons and astrocytes might exist in the brain and that this is mediated by the same agent – the excitatory amino acid glutamate. Indeed, it is now firmly established that glutamate released from synaptic terminals can activate ionotropic and metabotropic glutamate receptors on astrocytes, triggering elevations in the intracellular concentration of Ca^{2+} ([Ca^{2+}]_i) in these cells3-4. But astrocytes can also talk back to neurons by releasing glutamate, which acts on glutamate receptors on neurons5-6. The activation of glutamate receptors results in elevations in [Ca^{2+}]_i that might exert multiple actions on neuronal function. Indeed, the authors highlight the recent evidence obtained from both neurone–astrocytes co-cultures and acute brain-slice preparations for the involvement of glutamate release from astrocytes in the modulation of neuronal excitability and synaptic transmission.

Astrocytes are accurate sensors of neuronal activity

I should like to discuss a few aspects of the reciprocal signalling between neurons and astrocytes, including the possible rules governing these interactions, which were not addressed in depth in the Gallo and Ghiani review. It is worth underlining that although we would not expect this form of bidirectional signalling to represent a mode of information transfer as rapid as neuronal synaptic transmission, it is certainly possible that it does carry some relevant pieces of information. This raises several questions. Under what conditions can the glutamate released from synaptic

Daniele Piomelli
Professor, E-mail: piomelli@uci.edu
Andrea Giuffrida
Researcher, Department of Pharmacology, University of California, Irvine, 380 MSR II, Irvine, CA 92697-4625, USA. E-mail: agiuffri@uci.edu

References