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INTRODUCTION

Non-Benzodiazepine Anxiolytics and Hypnotics

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I am pleased to welcome all the participants and to introduce this symposium dealing with the preclinical and clinical aspects of non-benzodiazepine anxiolytics.

This meeting can be considered as a continuation of another symposium on the same topic ("Benzodiazepine-Receptor Modulation by Non-Benzodiazepine Anxiolytics") which took place three years ago in Florence in occasion of the CINP Congress. Publication of the proceedings of the Florence symposium (*Pharmacol Biochem Behav* **23**: 637–694, 1985) was well received and we therefore felt encouraged to organize another meeting on the subject. Moreover, during these years evidence accumulated, suggesting that an alternative strategy for the therapy of anxiety and sleep disorders indeed exists and is worth of pursuit, and we are here to assess the present status of the art with the help of an international team of experts.

This is the first meeting held in our Institute dedicated to a defined topic of pharmacotherapy. As you know, the Istituto Superiore di Sanità is directly involved in several aspects of the regulatory activities related to the National Health Service. Among them, it has been in charge, since 1977, of the processing of applications for the clinical trials of new drugs. We therefore very often face problems of previsional pharmacology, namely the rationale for several pharmacological tests to predict an effect for a new drug in the clinic. We are therefore particularly interested in organizing meetings aimed at providing a survey of the current status of knowledge in the various fields of therapy.

There is a general consensus that 25 years ago the introduction in the clinical practice of the benzodiazepines opened a new avenue in the management of anxiety and insomnia. Research on compounds endowed with selectivity of action on the various types of receptor for the benzodiazepine indicated the possibility (although only theoretically at present) that distinct receptor types of the benzodiazepine can subserve specific effects. This should lead to the identification, through "in vitro" screening tests, of drugs possessing selectivity for either anxiolytic or hypnotic action and deprived of the unwanted effects of these drugs. This kind of approach has to be encouraged, in view of the possibility to reduce the use of animals for the "in vivo" studies.

The pharmacological tests "in vivo" will thereafter confirm the mechanism of action of the new compound, its pharmacological profile and its probable clinical application. These "in vivo" studies are hindered by the scarce predicting value of the various tests in use, which recognize the anticonflict, sedative, myorelaxant and anticonvulsant properties of a new compound. The various paradigms that appear to have a considerable specificity indeed present several inconsistencies if not inserted in a correct strategy. New drugs can have effects similar to those of the classical anxiolytics in some situations, but not in others. On the contrary, several drugs can have anxiolytic activity in humans, but are endowed with a pharmacodynamic profile different from classical anxiolytics. This may be due to the ability of the drug to act at different points of a functional chain within a given regulatory system, which possesses a plurality of mechanisms. Actually, encouraging results derive from studies with drugs that influence serotonin- and dopamine-mediated transmission. It seems, therefore, not correct to study a putative anxiolytic only as a function of its ability to enhance γ-aminobutyric acid transmission in the central nervous system.