



MONOGRAPHS OF
THE MARIO NEGRI INSTITUTE FOR
PHARMACOLOGICAL RESEARCH, MILAN

Factors Affecting the Action
of Narcotics

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Factors Affecting the Action of Narcotics

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Preface

Despite their serious drawbacks of tolerance and dependence, whose nature has still to be fully elucidated, and the allied problems of abuse, natural and synthetic drugs with morphine-like action, that is, narcotics, retain a very important place in therapy, especially in the treatment of pain.

Like the majority of drugs, narcotics elicit their pharmacological effects by interacting with specific receptors. Indeed one of the major recent efforts in narcotic research has been to characterize these receptors on the basis of the *in vitro* stereospecific binding of high specific activity labelled opiates. Even more recently this has progressed to the isolation of endogenous ligands, that is, physiologically occurring peptides with morphine-like action, a development that in turn has provided considerable openings, and is authoritatively reviewed in this volume.

Specific interaction at receptors may be considered the central event leading to the characteristic biological responses to administration of narcotics. Yet several other steps, either previous or subsequent to receptor activation, are likewise critical as regards the end results. The different levels and the various mechanisms involved are related in a complex cause-and-effect chain, each link potentially influencable by the experimental variables. Recognition and control of these factors, and awareness of the difficulty of varying only one of them at a time, are among the requisites of a scientifically correct approach to the question in laboratory investigations. Similarly, well controlled studies of the physiological and pathological entities modulating the effects of narcotics in man, as well as of drug interactions of clinical significance, are highly desirable.

This monograph contains the proceedings of a meeting held at the Mario Negri Institute for Pharmacological Research to review current information on the pharmacology of narcotics from a different perspective. The idea behind the organization of the meeting was in fact to provide a novel view of the considerable variety of modes of action of narcotic drugs, both in laboratory animals and at the clinical level, in order to better define the underlying factors.

The meeting represented a unique opportunity for discussion and exchange between scientists who take different but parallel approaches in their work on narcotics, and among whom there is limited cross-communication as a result of today's increasing tendency to narrow specialization.

Besides providing new insights and information, and — we hope — stimulating further research, this work should prove its worth as a lasting reference text.

Italy is now facing domestic escalation of the serious worldwide medical and social problem of opiate abuse: an estimate of ten thousand heroin addicts in the

city of Milan, most of them under twenty years of age, speaks for itself. The gathering in our Institute of so many experts in the pharmacology of opiates, from different parts of the world, also bears witness to their belief that biomedical research plays a fundamental role in our endeavors to protect society from the modern epidemic represented by drug abuse.

On behalf of the Mario Negri Institute, it is my privilege to gratefully acknowledge the substantial contribution made by the authors, and the cooperation of all those who worked to render the meeting possible.

Luciano Manara

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