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MEETING REPORT

Benzodiazepine-Receptor Modulation by Non-Benzodiazepine Anxiolytics

Symposium held June 23, 1984

CINP Congress
Florence, Italy

Chairmen

Leonard Cook
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WE are pleased to present this symposium describing the pharmacology of non-benzodiazepine anxiolytic agents. It is our purpose to place the pharmacological effects of these newer anxiolytic agents in perspective compared to typical benzodiazepine pharmacology and mechanisms of action.

This symposium demonstrates that the pharmacological actions producing therapeutic efficacy in alleviating anxiety may be produced by several types of chemical classes, and clearly are not restricted to only benzodiazepines.

Typically, benzodiazepines produce a broad spectrum of pharmacological effects which include both desirable and undesirable actions. Significant efforts have been made by many laboratories to identify benzodiazepines with more specific pharmacological actions in order to reduce generally associated undesirable effects. These efforts have included compounds with mixed agonist and antagonist properties, which was the subject of another symposium at this meeting. A major thrust in research with benzodiazepines was generated by the identification of receptors to which many benzodiazepines bind. Since the majority of active ligands studied during these studies were benzodiazepines, it has been common to refer to these binding sites as "benzodiazepine receptors." Attempts have been made to identify subsets of these "benzodiazepine receptors" as being associated with specific aspects of their broad pharmacological profile, such as antianxiety or sedative or muscle relaxant properties.

The contributors of this symposium describe the pharmacology of non-benzodiazepines representing several different chemical classes and how they produce pharmacological profiles qualitatively similar to the benzodiazepines. Most of these agents also bind to the same receptors that benzodiazepines do. Some of these newer chemical series also possess both agonist as well as antagonist pharmacological properties; therefore, these dual effects are not unique to the benzodiazepines.

In regard to whether certain subsets of "benzodiazepine receptors" are key to producing antianxiety properties, let us not overlook the fact that agents such as meprobamate, barbiturates and compounds described in this symposium also produce antianxiety effects and do not bind to these specific "anxiety-antianxiety receptors." It is also clear that antianxiety effects can be maintained, while other effects usually associated with benzodiazepines can vary, which underscores the independence of specific antianxiety properties. In this regard, it appears that alcohol potentiation and sedation may be produced independently from effects predictive of antianxiety properties. Additionally, these presentations demonstrate differences in drug dependence properties among these anxiolytics in animals studies.

Future research with anxiolytic compounds will probably confirm specific binding associated with specific pharmacological properties, and we believe that it will no longer be appropriate to identify such receptor binding sites as "benzodiazepine receptors." Even at this point in time, we are well beyond only having a single chemical class associated with these particular binding sites.

This symposium describes new opportunities for identifying different chemical classes that produce, in animals, specific aspects of benzodiazepine-type pharmacology. Clearly, it is feasible to expect that additional new chemical classes will be clinically effective as anxiolytics and perhaps with greater specificity and less side effect profiles than present day "benzodiazepine standards."