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# MEETING REPORT

## Symposium on Recent Developments in the Study of the Mechanisms of Benzodiazepine Actions

Maui, Hawaii

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In spite of their pre-eminence among drugs prescribed for psychotherapeutic action, the mechanism of action of the benzodiazepines (BZ) has remained elusive. The recent finding of stereospecific, high-affinity binding of BZ to synaptosomal membrane fractions has generated much excitement on the part of workers interested in determining the neurochemical substrate underlying their actions. The work presented in this symposium, will address three significant questions concerning the role of BZ receptors in the CNS.

The first question relates to the *pharmacological* significance of these receptors. The effects of the benzodiazepines are manifold; including disinhibition of suppressed behavior, stimulation of consummatory behavior, facilitation or inhibition of aggressive behavior, muscle relaxant properties, anti-convulsant and hypnotic activity. Can interactions with a single population of receptors explain all of these effects or do different populations exist? May some of these effects be explained in interaction with glycine or gaba receptors?

Second, we must address the question of the *physiological* significance of these receptors. What is their anatomical and cellular localization? Do they occur on glial as well as neuronal elements? What are their dynamics and how are they regulated? Are second messengers involved? And of course, of primary interest and importance, what naturally-occurring substances interact with them? What is the nature of the endogenous ligand(s) and how do the BZ relate to these potential transmitter candidates? We don't know as yet if BZ behave as agonists or antagonists.

Finally we must consider the *clinical* relevance of these receptors. Here we are presented with an interesting paradox. The barbiturates are nearly indistinguishable from BZ in terms of their basic and clinical pharmacology—differences are primarily qualitative—yet they appear not to interact with BZ receptors. How are their effects mediated? Might we still find a role for 5-HT?

I would hope that this symposium provides some answers to these questions. I am reminded, however, of Claude Bernard's aphorism which suggests that the most worthwhile experiments are those that raise more questions than they answer.

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