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Proceedings From Workshop on 'Benzodiazepines, 5-HT & Anxiety'

For more than a decade it has been hypothesised that the anti-anxiety action of the benzodiazepines might be mediated by a reduction in serotonergic function. However, the evidence to support this hypothesis is both conflicting and controversial. In this workshop, Johnston and File review the effects in animal tests of anxiety of manipulating serotonergic function and the biochemical effects of benzodiazepines. Thiebot presents evidence to suggest that the effects on punished behaviors of reducing 5-HT function is not so much a reflection of anxiolytic action as an inability to wait, i.e., to tolerate a delay in reward. Gardner discusses several novel, non-benzodiazepine, compounds with some specificity for sub-types of 5-HT receptors. Unfortunately, even with the introduction of more specific pharmacological tools it remains impossible to draw any firm conclusions about the role of 5-HT in anxiety. Jones *et al.* examine the problem by studying the effects of a benzodiazepine inverse agonist, which has anxiogenic effects in animal tests. They conclude that the dorsal raphe nucleus is an important site mediating this effect. Finally, Nutt *et al.* report the effects in volunteers of acute and chronic administration of diazepam. Acute administration of diazepam inhibited the prolactin response to a challenge with l-tryptophan, but tolerance developed to this. They speculate that the mechanism underlying this tolerance is reduced 5-HT uptake, leading to enhanced post-synaptic receptor sensitivity.

Our discussions during the workshop led to the tantalising conclusion that the position was little clearer in 1985 than it had been in 1975. Hopes continued to be raised by positive results, only to be dashed by subsequent conflicting data. The role of 5-HT in anxiolytic drug action remains unknown, but nor are we able at this point to conclude that it plays no role.

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