

MEETING REPORT

Collegium Internationale Neuro-Psychopharmacologicum 13th C.I.N.P. Congress

Variability in Responses to Benzodiazepines¹

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THE purpose of this symposium was to examine the extent and nature of variability in responses to benzodiazepines. Many of us who work with benzodiazepines are aware that some individuals show little or no response to these drugs (e.g., [2]). This problem is usually overcome by rejecting poor responders on the basis of a pilot dose [4,7], or by increasing the subject numbers and/or the dose in order to obtain overall statistical significance. Little attention has been paid to the underlying causes of individual variability. This, of course, is of interest only if a "strong" or "weak" response to a benzodiazepine is a stable characteristic of an individual; the data presented from experiments in the rat [5] demonstrate significant stability. A separate point of interest is whether a "strong" or "weak" response to benzodiazepines is a general characteristic of an individual, which will be reflected in a wide range of behavioural and physiological responses; the papers by Bond and Lader and File [1,5] provide data on this question. There is a high correlation between physiological responses to benzodiazepines in man, and between closely related behavioral measures in both man and rat, whereas the correlations in benzodiazepine effect across different classes of response are lower. Possible explanations for these behavioral differences have been sought in the different sub-types of benzodiazepine receptors [3] and in their coupling with the GABA-system [8]. The extent to which behavioral differences can be attributed to pharmacokinetic differences is examined in the rat [5] and in man [6].

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REFERENCES

1. Bond, A. J. and M. H. Lader. Correlations among measures of response to benzodiazepines in man. *Pharmacol Biochem Behav* **18**: 295-298, 1983.
2. Cochrane, L. A., A. N. Nicholson and B. M. Stone. Variability of response to hypnotics: Sleep studies in man. *Pharmacol Biochem Behav* **18**: 307-310, 1983.
3. Dubnick, B., A. S. Lippa, C. A. Klepner, E. N. Greenblatt and B. Beer. The separation of ³H-benzodiazepine binding sites in brain and of benzodiazepine pharmacological properties. *Pharmacol Biochem Behav* **18**: 311-318, 1983.
4. Dika, T., R. Cumin, W. Haefely, A. Herz. Naloxone blocks the effects of diazepam and meprobamate on conflict behavior in rats. *Pharmacol Biochem Behav* **15**: 115-117, 1981.
5. File, S. E. Variability in behavioral responses to benzodiazepines in rats. *Pharmacol Biochem Behav* **18**: 303-306, 1983.
6. Greenblatt, D. J., R. I. Shader, M. Divoll and R. M. Arendt. Acute and chronic adaptation (tolerance) to the central depressant effects of benzodiazepines. *Pharmacol Biochem Behav*, in press.
7. Polc, P., E. P. Bonetti, L. Pieri, R. Cumin, R. M. Angioi, H. Mohler and W. E. Haefely. Caffeine antagonises several central effects of diazepam. *Life Sci* **28**: 2265-2275, 1981.
8. Simmonds, M. A. Variations in response of the GABA-picrotoxin-benzodiazepine receptor complex to flurazepam. *Pharmacol Biochem Behav* **18**: 299-301, 1983.

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