

Problems associated with the statistical analysis of drug interactions

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Investigations into the effects of one drug on the pharmacological properties of another are often complicated by the fact that both drugs may influence the parameter studied. In such cases this must be taken into account in the statistical analysis of the data.

We have met this problem while comparing the effects of a variety of drugs on the hypokinesia induced in mice by intraperitoneal injections of tetrabenazine and intracerebroventricular injections of noradrenaline hydrochloride.

Motor activity is at the best of times an extremely variable parameter, but the use of large numbers of observations coupled with a powerful statistical technique has enabled us to tackle the problem of analysing drug interactions with fair success. We have used a factorial design in our experiments and the data have been analysed using the analysis of variance (Kinnard & Watzman, 1966).

For our purposes a programme has been written (by B.D.T.) for an Elliott 803B computer which allows analysis of the data without transformation or in one of five (x^{-1} , $x^{-\frac{1}{2}}$, x^0 , $x^{\frac{1}{2}}$, x^2) transformations (Tukey, 1957).

The programme additionally includes tests for non-additivity and non-homogeneity of variance. The three basic assumptions of additivity, homogeneity of variance and normality underlying the analysis of variance (Snedecor, 1956) have been found to be most consistently satisfied by the use of the logarithmic transformation.

Details of the programme will be available and the method of its application and interpretation will be presented using our own experimental data.

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Relative potencies of sympathetic amines in human smooth muscle

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The classification of α - and β -adrenoreceptive receptors is based on: (a) the order of potency of sympathomimetic amines in evoking these responses, and (b) the ability of adrenergic antagonists to block these responses. Although Bennett & Whitney (1966) have shown the existence of α - and β - inhibitory receptors in human gastrointestinal tract by the use of α - and β -receptor antagonists, the use of order of potency as a criterion for classification in human tissue has not received much attention.

The order of potency of adrenaline, isoprenaline and phenylephrine relative to noradrenaline (1.00) in human smooth muscle from various tissues has therefore been studied. Fresh surgical specimens were dissected free of superfluous tissue and suspended in an organ bath at 37° C. In all experiments the Krebs bicarbonate solution included cocaine HCl (5 μ g/ml.) to block the amine uptake mechanism of the sympathetic nerve terminals, propranolol HCl (0.5 μ g/ml.) to block β -adrenoreceptive receptors (except in artery and vein), and for ileum, colon and rectum