The results of such studies can often be interpreted phenomenologically in terms of the Michaelis-Menten equation. Linear, and non-linear fits to this equation have been made using both established, and also novel computer programs written in Fortran IV and run on the University of London CDC 6600 computer. Graphs of three linear transforms of the Michaelis-Menten equation have also been constructed using a CalComp incremental graph plotting machine.

In addition, a study has been made in order to determine the components of the experimental variance, and the extent of their contribution to the results has been assessed. Kinetic analysis indicated that the uptake of all the amino acids exhibited non-linearity when plotted according to the various linear transforms of the Michaelis-Menten equation, and showed both low and high affinity components (Table 1).

TABLE 1. *Apparent Km values (μM) for amino acid uptake by the retina. Tissue was incubated with the labelled amino acids for 5 min. and the accumulation of radioactivity was used to obtain estimates of the initial velocity. Nine concentrations of amino acid were used to construct each plot (Lineweaver-Burk) and each point was the mean of 6–12 determinations*

Amino acid	Km_1	Km_2
Taurine	27	537
GABA	47	241
L-Aspartate	26	687
L-Glutamate	21	617
Glycine	7	1093
L-Alanine	13	440
L-Valine	119	403

The results obtained from these graphical methods have been compared with those computed from non-linear iterative fitting procedures assuming either one or two component uptake systems corresponding to the equations:

$$v = \frac{Vmax.\,S}{Km + S} \text{ and } v = \frac{V_1max.\,S}{Km_1 + S} + \frac{V_2max.\,S}{Km_2 + S} \text{ respectively.}$$

R. D. W. is an MRC Scholar. We are grateful to the S.K.F. Foundation and to the University of London, Central Research Fund, for grants to M. J. N.

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A theoretical model of ion-movements in micropipettes occurring during the course of microelectrophoresis experiments

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We have found that both parameters (intensity and time of application) of a prior retaining current are important in influencing the time-course of neuronal responses to microelectrophoretically applied drugs. Measurement of the amount of drug released by an ejecting current after the application of a retaining current suggested that retaining currents interfere with the kinetics of drug release (Bradshaw, Roberts & Szabadi, 1973). We demonstrate a theoretical model in an attempt to explain these experimental findings.

When the tip of a micropipette is immersed in an external medium (collecting fluid, brain tissue), a concentration gradient is set up between the drug solution and the

external medium, and diffusional release starts immediately. After some time a steady-state rate of diffusional release is established. At this stage, two 'concentration layers' exist within the tip of the micropipette: (1) the bulk of the drug solution, where the concentration of drug molecules is uniform, (2) an interphase layer, where the concentration gradually decreases towards the external medium (Ficks first law of diffusion).

When a retaining potential is applied to the drug solution, the drug ions drift away from the tip of the micropipette. This drift is not opposed by diffusion in the bulk of the solution, whereas in the interphase layer the net ion movement is the difference between the inward iontophoretic and outward diffusional ion fluxes. If the iontophoretic flux (R_i) is smaller than the diffusional flux (R_D), the retaining potential cannot counteract diffusional drug release instantaneously. However, the iontophoretic flux in the bulk of the solution gradually increases the thickness of the interphase layer, thus reducing the concentration gradient. Consequently, the rate of diffusional ion transport declines until $R_i = R_D$, and there is no diffusional release. Thus a retaining current, which initially is not adequate, can after some time ('minimal effective retention time') become effective. If a retaining current is applied longer than the minimal effective retention time, the whole interphase layer moves away from the tip, and the terminal part of the micropipette becomes depleted of drug ions.

When an ejected potential is applied, after a period of drug retention, the onset of release may be delayed ('release latency'), and it may take some time before a steady-state rate of release is established. The release latency corresponds to the time which is necessary for the interphase layer to reach the tip orifice, and the establishment of the steady-state rate of release reflects the arrival of the bulk of the solution at the tip orifice.

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The effect of anti-Parkinson drugs on catalepsy induced by α-methyl-*p*-tyrosine in rats pretreated with intraventricular 6-hydroxydopamine

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Catalepsy may be induced in rats by agents which impair dopaminergic function, such as reserpine or haloperidol. Surprisingly, α-methyl-*p*-tyrosine (αMPT), 250 mg/kg I.P., a specific inhibitor of catecholamine biosynthesis produces only a marginal catalepsy. Recently, Sayers & Spencer (1971) reported that high doses of dexamphetamine caused marked catalepsy in rats pretreated with αMPT. The effect was not attributed to depletion of dopamine (DA) since Corrodi, Fuxe & Hökfelt (1967) have shown brain DA concentrations to be little affected by dexamphetamine in αMPT pretreated rats. However, noradrenaline (NA) is reduced by dexamphetamine at high doses indicating that reduced NA may be a prerequisite for the induction of catalepsy with αMPT. In order to investigate this hypothesis we have selectively reduced brain NA in rats by the intraventricular injection of 6-hydroxydopamine (6-OHDA) (250 μg base). When αMPT (250 mg/kg I.P.) is given to these rats 10 to 15 days after 6-OHDA a marked catalepsy occurs, commencing about 4 h after dosing and lasting for over 24 h, during which time NA stores would be low and DA synthesis inhibited.

We have used the reversal of this long lasting catalepsy to characterize the action of a range of drugs, active in Parkinsonism and/or reserpine induced catalepsy in rats. Drugs were given 18 h after αMPT and catalepsy scored at half-hourly intervals for 4·5 h using the method described by Simon, Malatroy & Boissier (1970). Catalepsy was inhibited by amantadine (40 mg/kg S.C.), apomorphine (2·5 mg/kg S.C.), benztropine