concentration of guanethidine and block of reuptake of noradrenaline could contribute to the reversal of blockade by dexamphetamine.

The effects of amphetamine on the excretion of guanethidine in man have also been examined. It has been shown that, after the administration of 50 μCi of ^{3}H-guanethidine intravenously in man, the urinary excretion follows a bi-exponential course. The late exponential phase occurs after about 5 days following the injection and has a half-time of decay of 5·7 days. In three subjects, the administration of amphetamine 10 mg t.d.s., 8 days after the ^{3}H-guanethidine injection, caused a pronounced increase in the rate of excretion of ^{3}H-guanethidine. This implies that in man, as well as in the cat, amphetamines can enhance the removal of guanethidine from its site of action and may explain, at least in part, the mechanism of this drug interaction in man.

† Present address: St. Bartholomew's Hospital, London, E.C.1.

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The effect of nitrous oxide on reaction time and cerebral evoked potential

M. J. JARVIS and M. H. LADER, *Departments of Pharmacology and Physiology, University College, Gower Street, London, W.C.*1

There is evidence that certain later components of the electroencephalographic evoked response recorded from the vertex of the scalp reflect the levels of attention and alertness of the subject. Satterfield (1965) showed that the evoked response to an attended stimulus was of greater amplitude than that to an unattended stimulus. Similarly, the evoked response to signal stimuli is enhanced when the subject is required to discriminate between relevant and irrelevant stimuli during a prolonged visual vigilance task (Haider, Spong & Lindsley, 1964). Nitrous oxide, having depressant effects on central nervous system function, would be expected to decrease alertness and hence diminish the evoked response. In an earlier experiment, in which click stimuli were used to which the subject was not required to respond, diminution of all evoked response components between 40 ms and 240 ms after the stimulus occurred (Lader & Norris, 1969).

The experiment investigates the action of nitrous oxide further by examining its effects on reaction time performance and the evoked response to the reaction time stimulus. The experimental situation used is essentially similar to that in the study by Bostock & Jarvis (1969) in which the evoked response was found to vary according to the speed of reaction time, one component in particular, thought to relate to level of alertness, augmenting with slower reaction times. The subject is instructed to press a key as quickly as he can in response to the onset of a tone presented at random intervals through a loudspeaker behind his head. Fifty stimuli are presented at each dose level of nitrous oxide. The electroencephalogram is sampled and digitized every 2 ms for a 500 ms epoch after each stimulus. These data are stored together with the subject's reaction time on the Linc-8 computer digital magnetic tape. Averaging of the responses and analysis of the data is carried out off-line

by the computer at the end of the session. During each inter-trial interval (4–8 s) the previous trial's data are displayed by the computer on its oscilloscope.

Four concentrations of nitrous oxide in oxygen are used, 0, 10, 20 and 30% in a fully balanced order across subjects. The drug concentration is controlled using anaesthetic machine rotameters and is administered to the subject through an aviation-type face mask. At each dose level 10 min is allowed to elapse before recording, in order for equilibration of the gas to occur. The subject can communicate with the experimenter by means of a microphone in the mask.

Preliminary analysis confirms the earlier finding that all the main components of the vertex evoked response are diminished in a regular linear fashion with increasing dose levels of the drug. As expected, reaction time is prolonged by nitrous oxide. However, the component, which in the Bostock & Jarvis (1969) study did increase with lengthening of reaction time, paradoxically still shows this effect when the data are analysed in terms of speed of reaction time ignoring drug condition. This implies that the effects of nitrous oxide on such central functions as alertness and arousal cannot be entirely explained in terms of a simple depressant action.

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Pharmacological gadgets (T)

D. CARDINAL, T. HENSON and S. J. SMITH (introduced by A. F. GREEN), *Pharmacology Laboratory, Wellcome Research Laboratories, Beckenham, Kent*

A simple accurate injection gun for repetitive dosing (T)

D. FAULKNER and M. BENNIE (introduced by G. A. STEWART), *The Wellcome Foundation Ltd., Dartford, Kent*

Meter for measuring activity of small animals in metabolic studies (T)

D. FAULKNER and M. BENNIE (introduced by G. A. STEWART), *The Wellcome Foundation Ltd., Dartford, Kent*

The ventromedial nucleus of the hypothalamus and appetite control in the rat (T)

J. TRETHEWEY (introduced by G. A. STEWART), *The Wellcome Foundation Ltd., Dartford, Kent*

Whole body autoradiography (T)

D. A. FAREBROTHER and V. UDALL (introduced by M. WEATHERALL), *Pathology Department, Wellcome Research Laboratories, Beckenham, Kent*