These results may reflect a difference between the ways in which narcotic analgesics and narcotic antagonist analgesics interact with central tryptaminergic and cholinergic systems in bringing about their antinociceptive effects.

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Alterations in sleep/wakefulness cycle in rats following treatment with (+)-lysergic acid diethylamide (LSD-25)

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In behavioural studies (Loew, Depoortere & Vigouret, 1970) LSD-25 modified the composition as well as quality of sleep in rats. In particular, the drug appeared to change the quality of paradoxical sleep (PS). In this study, electroencephalographic recordings have been undertaken in order to confirm or refute the results of our earlier experiments.

LSD-25 tartrate (1 mg/kg, calculated as the salt) was injected intraperitoneally into adult male Wistar rats bearing chronically implanted electrodes for recording brain and muscle activity. Recordings were made in habituated rats during a 6 h period following injection. Control recordings were taken from the same animals on the day before drug administration.

Analysis of the total 6 h recordings revealed a 43% ($P<0.05$) increase in wakefulness which was associated with a reduction of 51% ($P<0.05$) in PS and of 18% ($P<0.05$) in slow wave sleep (SWS). More detailed analysis of the results showed that the increase in wakefulness was most prominent in the first hour. This effect gradually declined until hour 4, whilst in hours 5 and 6 no significant changes in the percentages of wakefulness and sleep were seen.

Qualitatively, the recordings showed that the time course of the drug effect was biphasic. In the first phase, lasting up to 2 h, ' aberrant behaviour ' (Dixon, 1968) was accompanied by a pattern of cortical arousal. The stereotyped head movements were preceded by short spindle bursts in the cortex and lateral geniculate body. The second phase began with the appearance of SWS and PS. In this phase, continuous spindle activity in cortical and lateral geniculate recordings during SWS, was most prominent during the third hour. The PS was associated with enhanced phasic activity in the visual system and increased rapid eye movement compared with that seen in control recordings.

Thus the results presented here confirm our earlier, behavioural observation that the quality of PS is modified by LSD-25, as evidenced by changes in visual system activity. Furthermore, such changes do not appear to be limited to a specific part of the sleep/wakefulness cycle.

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Convulsive effects of 4-deoxypyridoxine in photosensitive baboons (*Papio papio*)

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Baboons (*Papio papio*) from the Casamance region of Senegal when exposed to intermittent light stimulation (ILS) show myoclonus and electroencephalographic (EEG) signs of epilepsy. These responses vary from brief myoclonus of the eyelids associated on the EEG with fronto-rolandic spikes and waves, to sustained generalized myoclonus and, more rarely, tonic-clonic seizures (Killam, Killam & Naquet, 1967).

Extradural skull electrodes have been chronically implanted in ten such baboons (adolescents, weights 4·5–6 kg) and the effects of ILS observed before and at various intervals after the intravenous injection of 4-deoxypyridoxine hydrochloride (10–150 mg/kg).

Deoxypyridoxine (10–20 mg/kg) did not modify the responses to ILS. Myoclonic responses to ILS were enhanced 15 min to 2 h after deoxypyridoxine (40–60 mg/kg). Animals normally giving transient myoclonic responses showed rhythmic myoclonus of the eyelids and face continuing for several seconds after the end of ILS. In four out of six baboons after deoxypyridoxine (80–100 mg/kg) this self-sustaining myoclonus developed into a full tonic-clonic seizure at least once between 45 and 180 min after the drug injection.

The injection of deoxypyridoxine (105–150 mg/kg) not only enhanced myoclonic responses to ILS but also led to the appearance after 46–67 min of spontaneous seizures. These recurred every 10–15 min, and were often only partial. They commonly originated in, and were sometimes confined to, the occipital cortex.

An excess of pyridoxine given intravenously a few minutes before and after the deoxypyridoxine blocked both the enhancement of photosensitivity produced by deoxypyridoxine (100 mg/kg) and the spontaneous seizures produced by 150 mg/kg.

The effects of 4-deoxypyridoxine in *Papio papio* thus closely resemble those previously observed (Meldrum, Balzano, Gadea & Naquet, 1970) after isoniazid or thiosemicarbazide. All three drugs at low doses enhance the photosensitivity of these baboons and at higher doses induce seizures originating in the occipital cortex. It is probable that all three drugs produce these convulsive effects by interfering with the formation or action of pyridoxal phosphate.

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