

## Evidence for a persistent central depressant action seen after recovery from anaesthesia

K. THURÁNSZKY, G. RABLOCZKY AND A. KÉKES-SZABÓ

The fate of the classical adrenaline reversal in anaesthetised and in conscious cats was investigated. It seems that anaesthesia has some late effects on pharmacological responses that can be demonstrated for up to 72 hr after recovery of consciousness. The adrenaline reversal typical of the anaesthetised cat persisted for up to 72 hr after recovery of consciousness, thereafter the response to intravenous adrenaline was entirely pressor.

IT has been shown previously (Thuránszky, 1966a) that adrenergic blocking agents like dihydroergotoxine reverse the pressor effect of adrenaline in anaesthetised animals but that this is not so in non-anaesthetised animals.

We often observed in the animals after they had awakened from anaesthesia and when their behaviour was apparently quite normal, that the pressor effect of adrenaline remained reversible by dihydroergotoxine. We decided to follow the response to adrenaline after dihydroergotoxine-pretreatment to see for how long after recovery from anaesthesia the response remained reversed.

### Experimental

#### METHOD

The blood pressure of cats in anaesthesia and during and after the awakening period was recorded by Thuránszky's method (1966b).

After awakening, the animals were regarded as normal if the behavioural responses, feeding habits and blood pressures responses evoked by exteroceptive stimuli appeared to be the same as those of animals which had not been anaesthetised (Thuránszky, 1966c).

The variations of the pressor effect of adrenaline in a dose of 10  $\mu\text{g}/\text{kg}$  were investigated under ether or hexobarbitone anaesthesia and at various intervals after awakening. The cats were all pretreated with dihydroergotoxine.

One of our experiments made during and after hexobarbitone anaesthesia is shown in Fig. 1. In panel (1) the effect of adrenaline (10  $\mu\text{g}/\text{kg}$  i.v.) on the mean blood pressure of a cat anaesthetised with 0.1 g/kg hexobarbitone is shown. In (2) is recorded the effect of the same dose of adrenaline after intravenous pretreatment with 0.5 mg/kg dihydroergotoxine. In panels (3)-(6) are shown the responses to 10  $\mu\text{g}/\text{kg}$  adrenaline given 15 min after 0.5 mg/kg dihydroergotoxine, recorded at 24, 36, 48 and 72 hr respectively after recovery from anaesthesia. The response was still reversed at 24 hr, biphasic at 36 and 48 hr and entirely pressor at 72 hr and subsequently.

In Fig. 2 the degree of elevation or depression of the blood pressure is demonstrated in mm Hg related to the starting blood pressure level. These animals were pretreated with 0.5 mg/kg dihydroergotoxine 15 min

From the Institute of Pharmacology, University Medical School, Szeged, Hungary.

PHARMACOLOGICAL EVIDENCE OF LATE EFFECT OF ANAESTHESIA

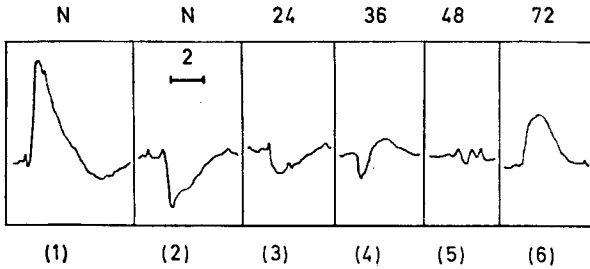


FIG. 1. Panel 1 shows the rise in blood pressure induced by 10  $\mu\text{g}/\text{kg}$  adrenaline given intravenously in a cat anaesthetised with hexobarbitone (0.1 g/kg). After 0.5 mg/kg dihydroergotoxine the response to the same dose of adrenaline was reversed (panel 2). Panels 3, 4, 5 and 6 show the gradual change in the response to adrenaline from adrenaline-reversal to an entirely pressor response in the cat at 24, 36, 48 and 72 hr after recovery of consciousness. The injections of adrenaline were given 15 min after pre-treatment with 0.5 mg/kg dihydroergotoxine. N represents the anaesthetised state. Time: 2 min.

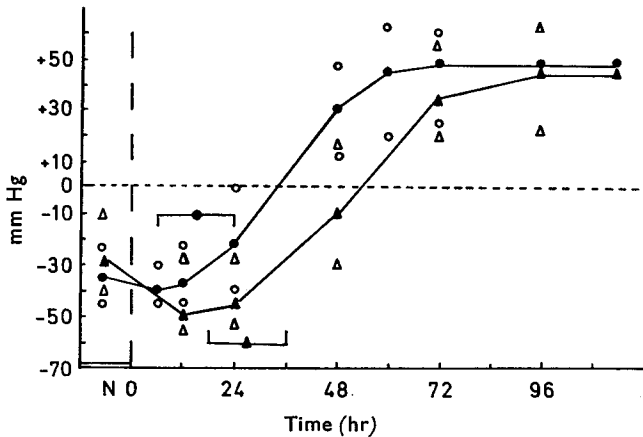


FIG. 2. The change in the response of the blood pressure of the cat to intravenous adrenaline after pretreatment with dihydroergotoxine, related to the anaesthetised state and the time after recovery of consciousness. Ordinate: change in b.p. in mm Hg; 0 is the baseline b.p.; + indicates a rise and - a fall in b.p. Abscissa: N is the anaesthetised state; 0 is the time of recovery of consciousness; 24, 48, 72, 96 hr after recovery of consciousness. Mean results obtained with ether as the anaesthetic are shown thus  $\bullet$ , and with hexobarbitone thus  $\blacktriangle$ . The bracketed circle and triangle show the period after awakening when the behavioural responses and blood pressure reflexes evoked by exteroceptive stimuli are normal. Open symbols show the range.

before each injection of adrenaline. The effect of adrenaline was investigated under ether or hexobarbitone anaesthesia and at various time intervals after awakening. It is obvious from Fig. 2 that there is a reversed effect of adrenaline both under anaesthesia with ether or hexobarbitone and in the early period after awakening.

After hexobarbitone anaesthesia the effect of adrenaline is still reversed after 48 hr, and becomes a pressor response only after the 72 hr. With

ether anaesthesia the reversed effect is abolished somewhere between 48 and 72 hr. In these experiments the anaesthesia persisted from 5 to 45 min. The variations of duration of the anaesthesia between such limits did not affect significantly the time for post-anaesthetic recovery of the pharmacological response mentioned above. Following a short-term anaesthesia with chlorethyl (shorter than 5 min) the effect of adrenaline became normal in 48 hr.

## Discussion

We conclude that there is a difference between the time necessary for post-anaesthetic recovery of behavioural responses and recovery of some pharmacological responses. The observation of the reversed effect of adrenaline produced by dihydroergotoxine is a suitable test to demonstrate the late effect of anaesthesia. It was reported by Thuránszky (1966a) that in conscious animals adrenergic blocking drugs could not reverse the effect of adrenaline whereas they reversed it in the anaesthetised state. In conscious animals adrenaline also produces a pressor response after administration of dihydroergotoxine. The present study makes it evident that after recovery from the anaesthetic it is possible to produce typical adrenaline-reversal with dihydroergotoxine, although at this time the animal is visually quite normal and awake and its behaviour and vegetative responses evoked by exteroceptive stimuli are normal, too. There is also a late effect of anaesthesia after 24 hr. The animal can only be regarded as normal pharmacologically when the typical adrenaline-reversal, after administration of dihydroergotoxine, has already disappeared and the adrenaline effect has returned to a pressor response. This total "awakening" takes places in the 72 hr after anaesthesia.

## References

- Thuránszky, K. (1966a). *Archs int. Pharmacodyn. Thé.*, **159**, 53-60.  
Thuránszky, K. (1966b). *Acta Physiol. Acad. Sci. Hung.*, **29**, 33-40.  
Thuránszky, K. (1966c). *Archs int. Pharmacodyn. Thé.*, **159**, 61-69.