

# REFERENCES

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## Partial adaptation to simulated time-zone shifts

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Two or three days after a time shift we have placed subjects under constant conditions for 24 hr and made hourly measurements of temperature and urinary excretion. These have been cross correlated with similar observations before time shift in four different ways:

- (1) with varying time shift as if the phase of the rhythm had altered;
- (2) with a mixture of the rhythm in the old and new phases in varying proportions as if two oscillators were additive, one in the old, the other in the new phase;
- (3) with a mixture of the unadapted rhythm and a rhythm adapted by a variable number of hours;
- (4) with a mixture of a fully adapted rhythm and a rhythm adapted by a variable number of hours.

The highest correlation has been accepted as the best descriptor of the state of partial adaptation.

Inferences about the process of adaptation to time shift can be drawn from these different descriptions of the state of partial adaptation. Since 3 or 4 was, in 173 out of 192 tests, the best descriptor, adaptation can best be described as involving two oscillators.

## How do rhythms adjust to time shifts?

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When circadian rhythms adapt to a time shift it is difficult to be certain whether the circadian clock has adjusted its phase or whether the measurable responses result simply from exogenous factors masking the influence of the clock. To throw light on this problem we have exposed twenty-four subjects to artificial time shifts of 8 hr advance or retard. One to three days later we have maintained these subjects under constant conditions for 24 hr, producing a urine sample and measuring rectal temperature hourly, taking small identical food and fluid intake hourly, and remaining awake and sedentary throughout the 24 hr. The data have been examined by cross-correlation (Mills, 1976).

On current hypotheses a partially adapted rhythm would be one in which the rhythms have moved less than the full eight hours of the time shift. For a westward shift this would represent a gradual lengthening of the period of the circadian rhythms, while for an eastward shift it would represent a gradual shortening. It is, however, conceivable that adaptation might take place by a shift of 16 hr 'in the wrong direction'.

Results suggested that adaptation commonly included a lengthening of the cycle, so that after the westward shift the phase gradually moved through eight hours, whereas after the eastward shift a lengthening by sixteen hours would be necessary before adaptation was complete.

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### **Dopaminergic influence upon the cerebral circulation in the anaesthetized baboon**

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The level of cerebral blood flow appears to be adjusted to the metabolic demands of cerebral tissue (Olesen, 1971; Risberg & Ingvar, 1973), although the mechanisms which ultimately trigger the changes in cerebrovascular resistance are still controversial. There have been few attempts to determine what influence dopamine exerts upon the cerebral circulation despite the reported importance of dopamine to cerebral function (Carlsson, 1972). It has also been suggested that cerebral blood vessels, particularly those in regions such as the caudate-putamen, may be innervated by dopaminergic neurones of an intracerebral origin (Hartman, Zide & Udenfriend, 1972). In the present study we examined in the baboon the effect upon cerebral blood flow and metabolism of both stimulation and blockade of dopamine receptors using apomorphine and pimozide respectively.

The surgical preparation of the baboon, anaesthesia and the measurements made, have been described in detail elsewhere (MacKenzie, McCulloch, O'Keane, Pickard & Harper, 1976). Cerebral blood flow (CBF) was determined from the externally monitored clearance of  $^{133}\text{Xe}$  following its injection into the internal carotid artery. The cerebral metabolic rates for oxygen and glucose utilization ( $\text{CMRO}_2$  and  $\text{CMR}_{\text{glu}}$ ) were estimated from the product of CBF and the arterio-venous differences of oxygen and glucose contents. Cerebral venous blood was obtained from the superior sagittal sinus.

Apomorphine (0.02–0.5 mg. kg<sup>-1</sup>, i.v.) administration resulted in highly