

storage form⁸—given 2 h before testing, also prevented the motor hyperactivity induced by morphine.

We conclude that at least some of the behavioural effects of morphine administration can be reversed by pre-treatment with drugs which affect biogenic amine metabolism. The specificity of some of these effects was demonstrated by their elimination when amine precursors (5-hydroxytryptophan and L-DOPA) were administered in conjunction with PCPA and AMPT, respectively. While no gross alterations of total biogenic amine levels have been found to result from single or multiple doses of morphine^{9,10}, the evidence for morphine-induced alterations in amine turnover rates is rather definite. Thus Gunne¹ and Haubrich and Blake¹¹ have shown that the brain levels and the urinary excretion of 5-hydroxy-indoleacetic acid and of catecholamine metabolites are increased substantially after administration of morphine, and Way *et al.* have shown increased accumulation of serotonin in morphinized animals treated with a monoamine oxidase inhibitor, compared with non-morphine treated controls². If increases in rate of turnover—rather than increases in the total (free and stored) levels—of the amines are the consequence of morphine treatment, two possible conclusions are suggested. Either the activities of rate-limiting enzymes concerned in the synthesis of the amines increase following morphine or, perhaps more likely, amine re-uptake into storage forms^{12,13} is impeded by morphine, thus increasing the amount of free amines available for synaptic transmission and metabolic degradation. Recent reports on the antagonism between reserpine and morphine^{14,15} and the interference we have found between imipramine and morphine support the second alternative, which also requires fewer assumptions. We now plan to test this hypothesis directly. If morphine is indeed found to interfere significantly with the uptake of serotonin and norepinephrine, our behavioural results would lead us to expect differences in the degree and duration of this interference, to account for the well known differences in the effects of morphine in tolerant and non-tolerant animals.

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Schizophrenia as a Genetic Morphism

THE incidence of schizophrenia in most communities is of the order of 1 per cent. Yet the fertility of schizophrenic males is low, as noted by Huxley *et al.*¹; and it has since been established that the fertility of schizophrenic females is low, too². The second observation serves to strengthen

the suggestion of Huxley *et al.* that the fertility of schizophrenics seems too low for the disorder to be maintained at its present rate by mutation alone. In explanation they noted the resistance of schizophrenics to surgical and wound shock, to visceral perforation, to high doses of histamine, insulin and thyroxine, and to pain. They noted also the possibility that schizophrenics may be resistant to diseases such as smallpox and bubonic plague which have occurred in widespread epidemics.

Moran³ suggested that the proposed robustness of the schizophrenic genotype might be manifested at an earlier stage of life: "I therefore suggest that the presence of a gene for schizophrenia has a protective effect for one or more of the genetic factors which cause the loss of fertilized ova".

It may be worth noting that the only two relevant studies known to me do not support Moran on this point. These suggested that, in contrast with control samples, there was a higher incidence of foetal loss among the sibs of schizophrenic propositi⁴, and that there was a higher proportion of miscarriages among the pregnancies of psychotic women (64 per cent of whom had been diagnosed as schizophrenic)⁵.

There are two problems about the incidence of schizophrenia: in the first place it seems very high, and in the second it seems not to be declining (as it should be if a schizophrenic gene protected its bearer against bubonic plague or smallpox). I can offer no fresh answer to the first. In regard to the second, it seems possible to me that either the level of schizophrenia is being maintained by an increasing degree of psychological stress to which we are said to be exposed, or that a true decline in schizophrenic rates is being masked by less extreme criteria of definition. Possibly one does not have to be so mad these days to be called "schizophrenic".

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Possible Relationships between Orienting and Diving Reflexes

THE diving reflex has been studied extensively in aquatic organisms that breathe air and submerge to obtain food or to escape from predators such as ducks, seals and alligators¹. This reflex seems to have two phases: an initial phase which may be mediated by the vagus and trigeminal nerves², and a later one which follows prolonged holding of the breath during voluntary or forcible submersion³. The initial phase includes bradycardia^{1,4}, apnoea (specifically, an interruption of respiration)^{1,4}, peripheral vasoconstriction^{4,5} and cephalic vasodilation⁵. Gaunt and Gans⁶ have reported that bradycardia in *Caiman crocodyli* is minimal during spontaneous dives but great during the approach of an investigator or during handling. They suggest that early diving bradycardia is mainly "psycho-genic" in origin and results from "threatening" stimuli. We have been studying (ref. 7 and unpublished results) the responses of the wholly aquatic salamander *Necturus maculosus* (mudpuppy) and have noted similarities to the early components of diving, specifically bradycardia and an interruption of respiration. (*Necturus* breathes through

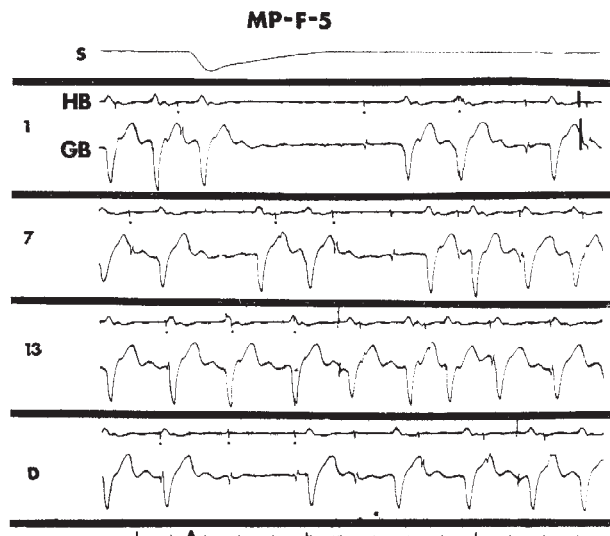


Fig. 1. The effect of repeated shadow stimulation on heart beat (HB) and gill beat (GB) in one animal. Passage of the shadow was recorded by a photocell on the aquarium (S). Initial shadow presentation (1) produced bradycardia and apnoea seen first as an interruption for about 4 s, followed by resumption at a slower and more variable rate. Repeated shadow presentation (at approximately 120 s intervals for this animal) led to a decrement in the degree of bradycardia and apnoea (trial 7) and finally to no effect (trial 13). The apnoea was reinstated by changing the shadow direction (D). Heart beats immediately before, during and after the shadow are denoted by dots. Bandpass: HB, 15–75 Hz; GB, 1–75 Hz. Calibrations, 10 μ V and 1 s.

large external gills beating back and forth at 0.5–1.0 beats/s.) Insofar as it does not dive, we suggest here that these responses of *Necturus* are components of the orienting reflex^{8,9} rather than the initial diving reflex, and that both reflexes may reflect some common neural substrate involving adaptive responses to external stimulation.

Necturus maculosus obtained from a commercial dealer were kept and tested in water at 19°C. Sixty animals were tested singly in a 'Plexiglas' aquarium, 28 × 12 × 6 cm, housed in a refrigerator. Dim illumination (2.5 foot lamberts at the aquarium) was provided by a parallel array of six luminescent strips (Sylvania 'Tape-Lite' PTL 175) mounted 30 cm above the aquarium. The illusion of a moving shadow was created over the aquarium by sequentially interrupting current to each strip with silent solid state circuitry¹⁰. The shadow velocity was 0.11 m/s. Respiration (gill beating) and heart beat were recorded, without affixing leads to the animal, by stainless steel studs (5 mm diameter) embedded in the sides of the aquarium below the surface. Voltages generated by water waves after gill beating, and EKGs recorded by volume conduction, were recorded via high gain differential amplifiers on a polygraph. We shall give a complete validation of the recording technique elsewhere (see also ref. 7). It has the advantage of working without sensors or restraint of the subject. One limitation is that gill and heart beats may be obscured during large movements, although the movements are revealed by their own characteristic voltages following water turbulence. Our data came from quiescent animals.

The animals equilibrated for at least 24 h before the shadow was first presented. After the first stimulus, respiration was interrupted, as could be seen from the cessation of gill beat in all animals, and bradycardia in 83 per cent, seen at first as one or more "skipped" beats. Periodic presentation (30–400 s) of the stimulus evoked the same responses but with less vigour, until neither apnoea nor bradycardia occurred (Fig. 1). We interpreted the waning response as habituation, because apnoea and bradycardia can be brought back by a fresh stimulus such as reversing the direction of the shadow or applying vibration rather than shadow. Extensive investigations of other

parameters, such as the interval between trials, confirmed the interpretation of habituation^{7,11}. Response habituation is characteristic of the orienting reflex^{8,9}. Interestingly, the orienting reflex includes the same characteristics as the early phase of the diving reflex: bradycardia¹², apnoea¹³, peripheral vasoconstriction⁹ and cephalic vasodilation^{9,14}. These and other similarities between the early phase of diving and the orienting reflex are summarized in Table 1, in which the duck and mudpuppy are compared. While some data are lacking, the close similarity of the reflexes seems obvious. We do not suggest that the initial phase of the diving reflex is identical to the orienting reflex, although it would be interesting to know whether any of the early components of "spontaneous" diving exhibits habituation.

Table 1. A COMPARISON OF COMPONENTS OF THE DIVING REFLEX IN THE DUCK AND ORIENTING REFLEX IN THE MUDDUPPY

	Early phase of "diving reflex": (<i>Anas</i> sp.), duck	"Orienting reflex": (<i>Necturus maculosus</i>), mudpuppy
1. Apnoea present?	+++ (ref. 1)	+++ (ref. 7 and unpublished results)
2. Apnoea after end-expiration?	++ (ref. 1)	++ (ref. 7)
3. Bradycardia?	+++ (ref. 1)	++ (ref. 7 and unpublished results)
4. Bradycardia or standstill at end diastole?	++ (ref. 1)	++ (ref. 7)
5. Peripheral vasoconstriction	+++ (refs. 5, 20)	+
6. Cephalic vasodilation	+++ (refs. 5, 12, 20)	(?)
7. Vasodilation also in masseter muscles and oesophagus	+++ (ref. 5)	(?)
8. Decrease in somatic myographic activity	+	+
9. Potentiated by struggle?	++ (ref. 22)	+++ (ref. 7)
10. Primary vagal mediation?	++ (ref. 22)	+
11. Blocked by atropine?	+	+
12. Habituates?	(?)	+++
	+++ , Always present.	
	++ , Usually present.	
	+, Suggested but not conclusively demonstrated.	
	+ (?), Seen in "diving" frogs; no data on <i>Necturus</i> .	
	(?), No data.	

Belkin¹⁵ has suggested that components of the diving reflex may have evolved as specializations from physiological responses to more general situations of external stimulation of an animal. *Necturus* occupies an evolutionary position in which components of the orienting response might include such primitive physiological responses. If the diving and orienting reflexes are so related they may be expected to have closely related neural substrates. We note that stimulating the midbrain produces components of the initial diving reflex and the orienting reflex^{16,17}; components of both reflexes have been elicited also from the amygdaloid nucleus^{16,18,19}. It would seem that the diving and orienting reflexes have enough in common to justify further thought on their interrelation.

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Reproductive Cycle of a Neotropical Insectivorous Bat, *Myotis nigricans*

REPRODUCTIVE patterns in bats fall into three main categories. A synchronous breeding season and mono-oestry is common in all holarctic bats¹. Continual asynchronous breeding is found in some tropical bats of the families Desmodontidae², Phyllostomatidae³, Pteropodidae, Emballonuridae and Molossidae⁴. In some palaeotropical bats seasonal polyoestry is the rule, with two synchronized breeding seasons each year^{4,5}.

Because of the rigorous environment of the temperate zone, parturition in holarctic bats is largely limited to May, June and July, when temperatures are mild and food is abundant. Most of these temperate zone bats belong to the insectivorous family Vespertilionidae. Neotropical bats which breed continually are either sanguivorous or frugivorous and are probably never exposed to a shortage of food⁶.

Myotis nigricans, the first neotropical Vespertilionid whose reproduction has been studied, has a fourth type of reproductive cycle. These bats breed continually during most of the year but become reproductively quiescent for about 3 months during the latter part of the rainy season (Fig. 1).

We examined reproductive tracts of more than five hundred *M. nigricans* from September 1968 to September 1969. Animals were collected at weekly intervals from roosts on Barro Colorado Island and the nearby town of Gamboa, Canal Zone. Pregnant females were taken in every month of the year except December. In November only a few pregnancies were noted, and all of those were near term in the first week of the month. After a 7 week period with no pregnancies, 63 per cent of the females collected during January were found to be pregnant. The first pregnancies were noted on January 3 and parturition began in the last week of February. This and subsequent observations lead us to believe that the gestation period for *M. nigricans* is near the 50–60 days reported for other members of the genus⁷. The three pregnancy peaks are about 3 months apart and our observations show that this is about the time needed for gestation and lactation of one litter. The animals tend to become less synchronized as the year proceeds, as shown by the fact that the peaks become progressively shorter, and there is always a certain number of pregnancies at any given time.

The curve for lactation is similar to that for pregnancy, but, of course, shows a time lag of one to two months. The total of the two percentages is sometimes more than one hundred, indicating animals that are both pregnant and lactating. Evidence for polyoestry consists of numer-

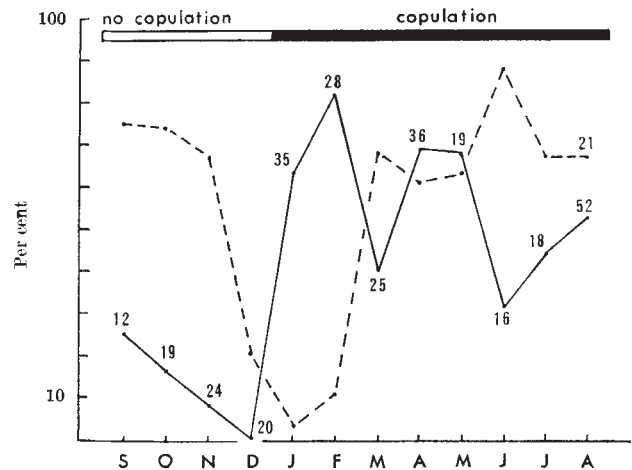


Fig. 1. Percentage of pregnant (—) and lactating (---) females in one year. The numbers are sample sizes.

ous individuals that were both pregnant and lactating, as well as continuous observations of banded individuals which produced at least two young during the year. This indicates post-partum oestrus at least occasionally, and we feel from other observations that it is the rule. This is the first conclusively demonstrated instance of polyoestry in the family Vespertilionidae, although there is suggestive evidence of its occurrence in a few Old World species of the genus *Pipistrellus*^{5,7}.

If the gestation period is less than 60 days, it is hypothetically possible for a given female to produce four young in a year. We feel that because of individual variation in times of copulation, ovulation, fertilization, gestation period and post-partum oestrus, three is a more usual number.

The fact that no young are produced from December to March may relate to seasonality of the food supply. During the dry season (January–March), insect populations are probably lower than at other times of the year⁸. There is usually an insect bloom in April when the rains begin. It seems that the strategy of the bats is to wean the young at this time of year and to avoid weaning young at times of lowered food supply. Copulation must therefore cease around the middle of September, and the last young of the year are born in November and weaned in December. Copulation begins again in January (we observed it many times). The first young are born in March and weaned in April. The cues for this cycle are as yet unknown, but the critical times are September and December, so that temperature and rainfall would seem to be extremely unlikely. Photoperiod is a possibility, but changes at this latitude are slight (1 h and 3 min from summer solstice to winter solstice).

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