performed by stripping both renal arteries and veins of their adventitia and coating them with a solution of 10% phenol in absolute alcohol for 5 min. Similar procedures have been shown to reduce kidney norepinephrine to undetectable levels as measured after 3–6 days[19] or 2 weeks[23]. Group II (n = 8) was subjected to a sham denervation, accomplished by exposing the renal vessels and applying an isotonic saline solution instead of phenol. Group III (n=5) was left untouched.

Arterial pressure and body weight were measured at weekly intervals starting 1 week after surgery, from 6 until 17 weeks of age. Blood pressure was measured by tail plethysmography in the awake, preheated rat[24]. At the end of the experiment, the rats were anesthetized with pentobarbital, 40 mg/kg, and the mean arterial pressure measured from a cannulated carotid artery. The animals were then sacrificed and the right kidneys excised and weighed. Results are given as means ± SE. Statistical comparisons were made using Student's t-test, and differences considered significant for a p-value less than 0.05.

Results and discussion. The figure illustrates the effect of bilateral renal denervation performed 5 weeks after birth on the development of high blood pressure in SH rats. Since there were no significant differences between sham-denervated and non-operated rats (groups II and III), these 2 groups have been combined and their arterial pressure compared with that of the denervated rats (group I). A significant difference existed between denervated and non-denervated rats from week 8 until week 13, the denervated rats having on the average a pressure 30 mm Hg below that of the non-denervated animals. From week 14 until the end of the experiment, the pressures were similar in the 2 groups. Direct measurement of mean arterial pressure at 17 weeks confirmed the absence of a significant difference in blood pressure between denervated and non denervated rats.

The figure also shows that between week 6 and week 9 there was no significant increase in blood pressure in the denervated rats, whereas a significant increase did occur in the non-denervated animals. On the other hand, a stable level of hypertension was achieved at week 12 in the non-denervated rats, but only at week 14 in the denervated group. Thus, hypertension was delayed by 2–3 weeks after renal denervation, but neither its rate of development nor its final level appeared modified by that procedure.

Body weight (b.w.) at the time of the denervation was 68.2 ± 2.1 g (group I); in group II and in group III at the same age, b.w. was 69.2 ± 2.8 and 67.5 ± 2.4 g respectively. Growth rate was significantly reduced in groups I and II compared to group III, especially during the first few weeks following surgery. At week 10, b.w. was 163.3 ± 8.0 g in group I, 174.4 ± 7.5 g in group II and 215.6 ± 5.5 g in group III, a value significantly greater than that of groups I and II. At the end of the experiment, b.w. was 294.2 ± 7.1 g in group III, a value still greater (although not significantly so) than that measured in group I (262.0 ± 11.7 g) or in group II (275.9 ± 6.0 g). As can be noted from these values, b.w. gain appeared also greater in group II than in group I, especially during the early period, although at no time were the differences significant. The weight of the right kidney at the time of sacrifice was not significantly affected by denervation (0.895 ± 0.041 g in group I vs 0.901 ± 0.030 g in group II).

These experiments indicate that bilateral renal denervation delays the development of high blood pressure in SH rats by 2–3 weeks. The experimental design does not permit us to answer several important questions concern ing the completeness and specificity of renal denervation, lack of systemic effects of phenol, and possible coincidence of reinnervation with the appearance of hypertension. Also, the study does not provide any explanation for the mechanisms which might link renal nerves to the appearance of hypertension in SH rats. Despite these obvious limitations, the present experiments may indicate an important relationship between sympathetic nervous system and renal function in SH rats pertaining to the hypertensive state.

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'Binding' of glycine and γ-aminobutyric acid to synaptosomal fractions of 6 regions of the feline brain; effects of strychnine[1]

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Summary. GABA (6×10^{-6} M) binding to synaptosome-enriched fractions of cat CNS exhibited a clear rostro-caudal gradient, whereas glycine (6×10^{-6} M) binding was greatest to particles of cerebellar cortex, and this was followed by medulla ≅ caudate nucleus ≧ cerebral cortex ≧ pons > corona radiata. Strychnine-SO_4 (10^{-3} or 10^{-4} M) inhibited the binding of GABA and glycine in all brain regions studied; at 10^{-5} M this drug inhibited the binding of both GABA and glycine only to particles of the cerebral cortex.

γ-Aminobutyric acid (GABA) and glycine may be inhibitory transmitters of the mammalian CNS[2–4]. Iontophoretic studies have revealed that the depressant action of GABA is more potent than that of glycine in higher structures of the CNS (e.g., cerebellar and cerebral cortices) than on lower centers, but that the action of glycine exhibits a reverse trend[3, 4, 5–8]. Therefore, central inhibitory mechanisms involving these amino acids might exhibit regional dependency. Recent studies which have shown that the 'binding' of GABA and glycine to various regions of the CNS appears to parallel their iontophoretic potencies, support this view[3, 9–13, 18]. In particular, it has been shown that a 'preferential binding' of GABA and glycine exists in synaptosomal fractions of rat cerebral cortex and spinal cord[10, 11, 18]. Other studies have provided further insight into the quantitative relationships which might exist between the depressant actions of these amino acids and the potencies of their mechanisms of receptor-interaction and 're-uptake'[14–18]. The present study was undertaken to compare the 'binding' of GABA

and glycine to synaptosomal fractions of 6 regions of the feline brain and to examine the effect of strychnine on these 'binding' mechanisms. Extensive studies on the binding of these 2 amino acids to particles of rat spinal cord have already been published[10,11,18].

Adult male cats (2.8–3.3 kg) were killed by injection of pentobarbitone-Na^+ (30 mg/kg, i.p.), followed by air embolism (saphenous vein). Their brains were exposed, and various cerebral structures were excised, weighed and homogenized in 10 volumes of ice-cold isosmotic (0.32 OsM) sucrose solution. All further operations were conducted at 0 °C. 4-ml-portions of homogenates (representing 0.364 g brain) were subjected to a previously-described subcellular fractionation procedure to prepare synaptosome-enriched 'P_2' fractions[11,18]. P_2 fractions were then re-suspended in 3.0 ml of glucose-free, bicarbonate-buffered medium[15], and 250 µl aliquots of these suspensions were pipetted into tared tubes, after which 250 µl of medium (drug-free, or containing 10^{-8} to 10^{-3} M strychnine-SO_4) were added to each tube. After mixing these suspensions and allowing them to stand for 10 min, 0.5 ml of a solution of equimolar concentrations of 1-^{14}C-glycine (16.7 Ci/m-mole; New England Nuclear Corp.) and 2,3-^{3}H-GABA (36.7 Ci/mmole; same source), in physiological medium, were added to each tube to provide final concentrations of 6×10^{-6} M of each amino acid. Samples were again mixed and allowed to stand at 0 °C for 15 min and then centrifuged at 17,000 × g, 30 min. Pellets were weighed and re-suspended in 2.0 ml of deionized water. Radioactivity due to ^{14}C and ^{3}H was determined in 0.5 ml aliquots of re-suspended pellets and in 100 µl aliquots of supernatant fractions using previously-described procedures[11,19]. The metabolism of glycine and GABA is negligible under conditions similar to those which were used herein[20,21]. The binding data were corrected for the amounts of ^{14}C-glycine and ^{3}H-GABA present in supernatant fluid trapped in the pellets using a previously-described method[11,18] and the ^{14}C-sucrose distribution ratios of the pellets. Sucrose distribution ratios, obtained in identical experiments were found to be 0.75 ± 0.02(26) for cerebral cortex; 0.84 ± 0.02(25) for cerebellar cortex; 0.79 ± 0.02(25) for caudate nucleus; 0.68 ± 0.01(26) for pons; 0.66 ± 0.01(27) for medulla oblongata; and 0.63 ± 0.01(24) for corona radiata (means ± S.E.M.; numbers of determinations in parentheses). The data shown in the table indicated that a 'preferential binding' of both GABA and glycine exists in the feline CNS[3,9–11,13,17]. The values for GABA 'binding' exhibited a clear rostro-caudal gradient, whereas glycine 'binding' occurred to the greatest extent in cerebellar cortex and this was followed by medulla ≅ caudate nucleus ≧ cerebral cortex ≧ pons > corona radiata. Strychnine-SO_4 (10^{-3} and 10^{-4} M) decreased the 'binding' of both GABA and glycine (both at 6×10^{-6} M) to particles of all brain regions studied, and at 10^{-5} M (a concentration close to that of the radioactive ligands), this drug significantly decreased the 'binding' of glycine to particles of cerebral cortex and that of GABA to particles of cerebral cortex and caudate nucleus. At 10^{-8} to 10^{-6} M, strychnine-SO_4 did not affect the 'binding' of GABA or glycine to particles of any of the brain regions studied (data not shown). These results confirm previous findings which have indicated that he 'binding' of GABA and glycine to synaptosomal particles of the mammalian CNS is regionally

Effects of strychnine-sulfate on the 'binding' of glycine and GABA to synaptosomal fractions of 6 regions of the feline brain

Brain region	Strychnine-SO_4 (M)	nmole/g P_2, in non-sucrose space ^{14}C-glycine	^{3}H-GABA
Cerebral cortex	0	24.5±0.7 (8)	55.2±1.0 (10)
	10^{-3}	6.9±1.1 (8)***	6.3±0.4 (8)***
	10^{-4}	14.9±1.6 (8)***	28.6±1.2 (8)***
	10^{-5}	20.1±0.9 (8)**	41.6±0.9 (8)***
Cerebellar cortex	0	44.2±3.5 (12)	63.5±1.1 (12)
	10^{-3}	14.5±3.3 (8)***	8.8±0.8 (8)***
	10^{-4}	32.0±3.2 (8)**	40.2±0.9 (8)***
	10^{-5}	43.8±4.8 (8)	59.8±1.4 (8)
Caudate nucleus	0	29.1±2.2 (10)	31.0±0.6 (10)
	10^{-3}	6.4±1.1 (8)***	3.3±0.2 (8)***
	10^{-4}	16.5±1.9 (8)***	18.3±0.7 (8)***
	10^{-5}	22.8±2.5 (7)	27.2±0.7 (7)**
Pons	0	22.7±1.6 (12)	15.5±1.2 (12)
	10^{-3}	5.7±0.7 (8)***	2.2±0.3 (8)***
	10^{-4}	14.5±1.5 (8)**	9.8±1.2 (8)***
	10^{-5}	20.6±2.2 (8)	13.6±1.4 (8)
Medulla oblongata	0	31.0±1.7 (12)	15.6±0.9 (11)
	10^{-3}	9.3±0.7 (8)***	2.2±0.1 (8)***
	10^{-4}	24.0±2.4 (8)*	9.6±0.6 (8)****
	10^{-5}	28.0±2.7 (8)	14.4±1.2 (8)
Corona radiata	0	11.4±0.3 (12)	3.4±0.1 (12)
	10^{-3}	2.4±0.2 (7)***	0.3±0.04 (7)***
	10^{-4}	6.3±0.3 (8)***	2.2±0.2 (8)***
	10^{-5}	10.4±0.5 (8)	3.3±0.2 (8)

Means ± S. E. M.; numbers of determinations in parentheses; *, ** and *** indicate, respectively, $p < 0.05$, $p < 0.01$ and $p < 0.001$, by comparison of these values with those obtained in the absence of strychnine-SO_4 (Student's t-test; two-tailed). All values were corrected for ^{14}C-glycine and ^{3}H-GABA present in trapped supernatant fluid of the pellets (see 'methods').

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dependent[3,9-11,13,18]. The finding that the potency of GABA 'binding' decreased from higher to lower CNS structures is in accord with its relative potency in iontophoretic studies[3,4]. The potency of glycine 'binding' was not so clearly related to its iontophoretic potency. Results with strychnine provided evidence for the lack of specificity of this agent[3,22,23]. Its inhibition of the binding of glycine and GABA indicates that it interacts with Na^+-dependent binding mechanisms involved in the uptake of these amino acids.

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Periodicity in body temperature in man

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Summary. Body temperatures and self-assessed mood scales were recorded for 7 weeks or more by male volunteers. Auto-correlations of temperatures from the 21 subjects show evidence of a significant peak at the 20-day-interval. The self-assessed measure of 'Alertness' (from 18 of them) also shows some evidence of rhythmicity, at the 22-day-period.

It is well-known that there are regular variations in body temperature in the human female, accompanying the menstrual cycle. Little is known about any analogous phenomenon in the male, despite the fact that there is some evidence of periodic (20-day) changes in urinary 17-ketosteroid excretion[1], and of a 20-day cycle in pitch perception[2]. The present study arose from the author's work on the 90-min Rapid Eye Movement sleep cycle (REMS/SWS cycle), using penile skin temperature as a measure of the erections accompanying REM sleep[3,4]. Frequency analysis showed little evidence of stable patterns of REM sleep over 17 weeks in 1 subject. However, taking average temperature values for each night, frequency analysis showed evidence of periodicity at 21 days. It was this tentative 'finding' which stimulated this subsequent experiment.

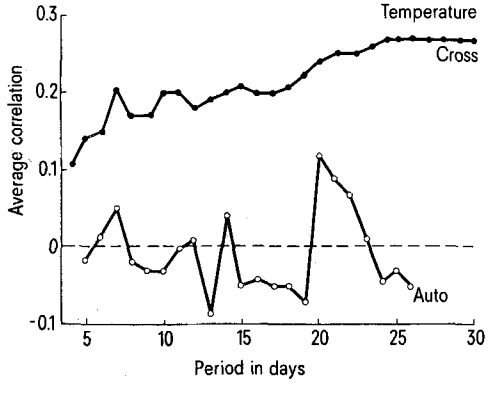

Fig. 1. Average auto-correlogram and cross-correlogram for temperature time series (N = 21).

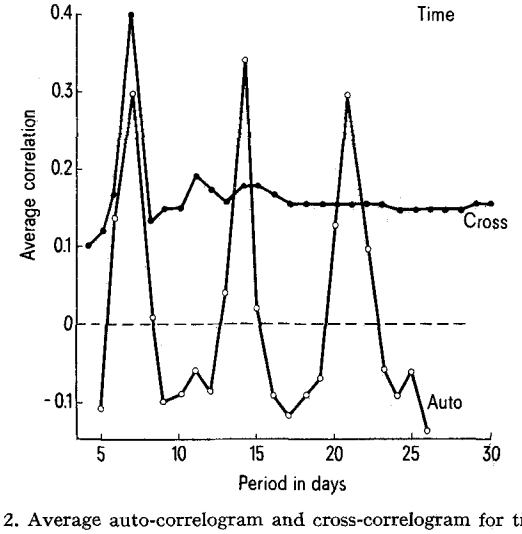

Fig. 2. Average auto-correlogram and cross-correlogram for time of getting up (N = 18).

Method. 21 male subjects, including undergraduate, postgraduate and staff members of the University of Hull, recorded their body temperature daily, for periods varying from 49 to 102 days. They were asked to continue for at least 7 weeks, and for as long as possible after that. 1 subject (the author) provided all-night average armpit skin temperatures. The others took their oral temperature with a clinical thermometer every morning, before getting up, noting the time at which the recording was made. 18 of them also provided estimates of their mood, and the previous night's sleep quality, using 4 10 cm analogue scales[5]. The 3 mood scales were labelled at each end with the adjectives found to be most highly loaded on the extremes of 3 major bipolar factors in mood, recently assessed in a British university population[6]. These scales could best be described as being 'Alertness-Dullness', 'Anxiety-Confidence and 'Elation-Quietness'. Subjects were instructed to complete the analogue scales as soon as they had got up.

Results. 18 subjects provided measures on each of 6 scales – temperature, time of recording, 3 mood scales and sleep quality. 3 others provided temperature measures only. Each number series was analyzed, using both auto-correlation and sinusoidal cross-correlation. (The analogue scale series were each ranked before analysis, as it is highly unlikely that subjects would be using strictly interval scaling in their self-assessments.)

Figure 1 shows the average correlograms for temperature, and it is apparent that there is a peak in the auto-cor-

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