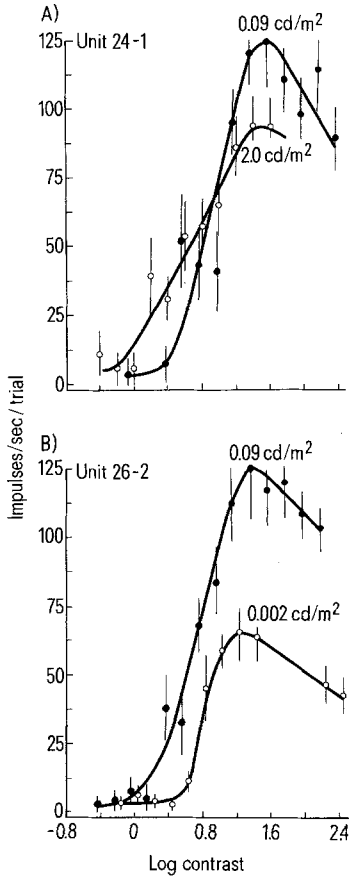
consequence of the effects described in a) and b), whenever the background luminance was raised, the contrast range over which the stimulus-response relation was obtained became wider; d) the magnitude (impulses/sec) of the maximal response was small at low background luminance (0.002 cd/m^2) and increased with background luminance levels up to 0.09 cd/m^2. Beyond this background level, the maximal response magnitude decreased progressively as luminance increased, at least within the range we explored (the highest background luminance tested was 2 cd/m^2); e) at background levels higher than 0.09 cd/m^2 the stimulus-response curves had a lower positive slope.

These results suggest the following comments. 1. The range of contrast which can be recognized by cortical neurons increases as a function of background luminance, at least within those background levels explored by us (0.002–2 cd/m^2). 2. Since the widening of the contrast range is due only to a shift to the left – that is to a lowering – of the threshold, the sensitivity of cortical visual neurons increases as a function of the background luminance. 3. Since at background levels higher than 0.09 cd/m^2 the stimulus-response curves had a lower positive slope, the resolution power for detecting differences in stimulus contrast decreases from this level (0.09 cd/m^2) up to the highest background we explored (2 cd/m^2). In conclusion, background changes can markedly modify important characteristics of the visual information process such as threshold and resolution power.



Stimulus-response function at different levels of background luminance. In *A* and *B* the levels of diffuse luminance of the tangent screen expressed in cd/m^2 are reported on the top of each curve. The unit in *A* was isolated in area 17, classified as simple cell and activated by 500-msec stationary flashes of light of variable contrast. The unit in *B* was isolated in area 18, classified as simple cell[8] and activated by 500-msec stationary 'negative' flashes of light of variable contrast; 'negative' flashes were obtained by switching off for 500 msec the light of the focal stimulus. In this case the contrast of the stimulus was again I-B/B where I was the light intensity of the focal stimulus before the switching off and B the background luminance. Each data point of the curves represents the mean ±SD of 10 random trials.

1 This investigation was supported by a grant from the Consiglio Nazionale delle Ricerche, Rome (Italy).
2 E. Riva Sanseverino, C. Galletti and M.G. Maioli, Electroenceph. clin. Neurophysiol. *34*, 739 (1973).
3 B. Sakmann and O.D. Creutzfeldt, Pflügers Arch. ges. Physiol. *313*, 168 (1969).
4 V. Virsu, B.B. Lee and O.D. Creutzfeldt, Exp. Brain Res. *27*, 35 (1977).
5 G.F. Poggio, F.H. Baker, Y. Lamarre and E. Riva Sanseverino, J. Neurophysiol. *32*, 892 (1969).
6 E. Riva Sanseverino, C. Galletti and M.G. Maioli, Brain Res. *54*, 225 (1973).
7 E. Riva Sanseverino, C. Galletti and M.G. Maioli, Brain Res. *124*, 251 (1977).
8 E. Riva Sanseverino, C. Galletti and M.G. Maioli, Arch Sci. biol. (Bologna) *58*, 1 (1974).
9 D.H. Hubel and T.N. Wiesel, J. Physiol. (Lond.) *160*, 106 (1962).
10 B. Dreher and L.J. Cottee, J. Neurophysiol. *38*, 735 (1975).
11 G.A. Orban, M. Callens and J. Colle, Brain Res. *90*, 205 (1975).

Effects of hypothalamic injections of 5,6-dihydroxytryptamine on thermoregulation in rats[1]

M.T. Lin

Department of Physiology and Biophysics, National Defense Medical Center, Taipei (Taiwan), 6 September 1978

Summary. 5,6-Dihydroxytryptamine, a serotonin depletor, infused directly into the anterior hypothalamus of rat's brain, produced an increase in both heat production and heat loss (as indicated by changes in peripheral circulation) at temperatures of 8, 15 and 22 °C. The rectal temperature of these treated rats remained constant.

Recently, a number of attempts to assess the thermoregulatory effects of a lowered content of 5-hydroxytryptamine (5-HT; serotonin) in the brain have produced conflicting results. For example, in rats in which brain 5-HT had been depleted by systemic administration of p-chlorophenylalanine, the rise in rectal temperature when exposed to the acute heat stress (38 °C) was reduced[2]. Both rats and monkeys treated with intrahypothalamic injection of 5,6-dihydroxytryptamine (5,6-DHT), a specific 5-HT depletor, were unable to maintain body temperature in the cold but recovered from the heat deficit[3,4]. On the other hand, the destruction of brain 5-HT neurons by pretreatment with intraventricular administration of 5,7-DHT, which lowered the brain 5-HT content, did not disrupt the thermal balance in rabbits[5,6]. Unfortunately, most of the experiments performed in studying the relation between brain 5-HT and thermoregulation have relied on measurements of rectal temperature solely. This makes it difficult properly to assess the action of brain 5-HT depletion on particular functions such as metabolic heat production, respiratory evaporative heat loss and vasomotor activity. This study was attempted to quantify any changes in the thermoregulatory outputs induced by the direct administration of 5,6-DHT into the preoptic anterior hypothalamus (POAH), in

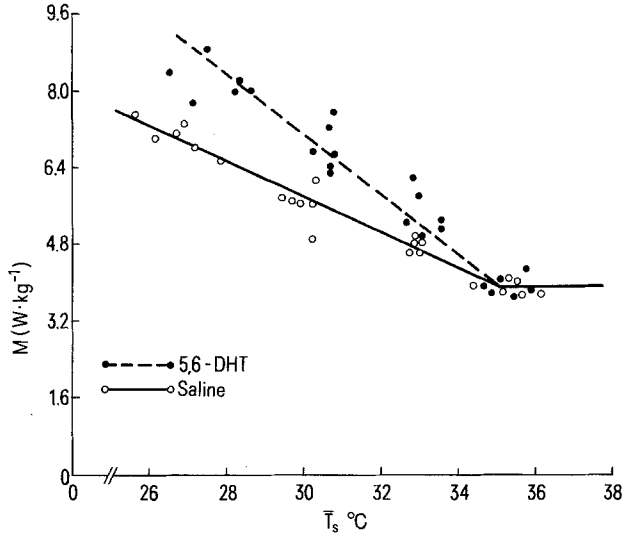
The thermoregulatory responses of 5,6-dihydroxytryptamine-(5,6-DHT)treated rats to ambient temperatures of 8, 15, 22 and 29 °C and the comparison of these responses to those of control rats

Treatment of animals	Number of animals	T_a, °C	T_r, °C	T_{bsk}, °C	T_f, °C	T_t, °C	$\bar{T}_s$, °C	M, W · kg^{-1}	E_{res}, W · kg^{-1}	k, W · m^{-2} °C^{-1}
Control	6	8	36.6±0.22	29.3±0.46	18.6±0.89	10.2±0.26	26.9±0.38	7.1±0.25	0.18±0.02	6.7±0.41
5,6-DHT	6	8	36.6±0.24	30.0±0.48	25.6±0.46*	12.1±0.23*	28.3±0.40*	8.1±0.27*	0.16±0.01	8.9±0.52*
Control	6	15	36.6±0.29	32.1±0.12	22.4±0.34	16.5±0.15	29.9±0.05	5.6±0.51	0.24±0.02	7.5±0.34
5,6-DHT	6	15	36.9±0.27	32.5±0.07	25.0±0.40*	18.9±0.13*	30.6±0.04*	6.9±0.45*	0.23±0.03	9.9±0.36*
Control	6	22	37.5±0.35	34.3±0.22	29.3±0.92	23.3±0.35	33.1±0.26	4.6±0.39	0.36±0.02	9.1±0.53
5,6-DHT	6	22	37.5±0.39	34.2±0.19	31.7±0.65*	25.0±0.33*	33.3±0.15	5.5±0.36*	0.37±0.04	11.2±0.42*
Control	6	29	37.9±0.37	35.7±0.41	34.8±0.33	31.0±0.43	35.2±0.36	4.0±0.35	0.71±0.04	11.2±0.63
5,6-DHT	6	29	38.0±0.35	35.8±0.28	34.5±0.30	30.8±0.38	35.3±0.20	4.0±0.25	0.63±0.05	11.7±0.71

Values are mean ± SE. * Significantly different from corresponding control group, $p < 0.05$ (Student's t-test).

order to identify the nature of the contribution that the hypothalamic 5-HT might make to thermoregulatory control.

Adult male Sprague-Dawley rats, weighing between 250 and 300 g, were used. The experiments were performed on the unanesthetized animals minimally restrained in rat stocks. 2 groups of animals were used: a) control rats which received an intrahypothalamic dose of saline vehicle, and b) rats which received an intrahypothalamic dose of 5,6-DHT (Sigma, 20 µg in 5 µl). Microinjections into the POAH were carried out according to the DeGroot[7] coordinates: AP, 7.0–7.1; Lat., 0.9–1.0; Hor., 0.01–0.1. A 27-gauge injecting needle was connected via PE 10 tubing to a 50 µl Hamilton syringe mounted on a specially constructed microinfusion pump. After the injecting needle was lowered to POAH, a volume of 5 µl was infused over a 30-sec interval and the needle was kept in place for 2 min before it was taken out of the brain. The vehicle for 5,6-DHT was 0.9% pyrogen-free saline to which 0.1 mg/ml of ascorbic acid was added. The animals treated with 5,6-DHT were studied between 2 and 6 days after the injections were made[8,9]. The thermal responses of these groups of animals to 4 different ambient temperatures (T_a) of 8, 15, 22 and 29 °C were observed. Metabolic rate (M), respiratory evaporative heat loss (E_{res}) and vasomotor activity were measured in a small animal partitional calorimeter which was originally developed by Hardy and his associates[5,10]. Metabolic rate was calculated in watts assuming an RQ = 0.83 so that 1 l of oxygen consumed per h was equivalent to a heat production of 5.6 W[5,11]. Respiratory evaporative heat loss (E_{res}) was calculated by measuring the increase in water vapor content in the helmet effluent air over that of the ambient air. Rectal (T_r), back skin (T_{bsk}), foot skin ($\bar{T}_f$) and tail skin (T_t) temperatures were measured using copper-constantan thermocouples. Mean skin temperature ($\bar{T}_s$) was calculated according to the equation: $\bar{T}_s = 0.83\ T_{bsk} + 0.10\ T_f + 0.07\ T_t$ (Lin et al., unpublished data). A measure of the tonus of the whole peripheral circulation can be obtained by calculating a conductance (k) value for the core to skin heat flow. With the exception of the E_{res}, all heat leaving the animal's body must pass from the core to the skin. Furthermore, under steady-state conditions, when heat storage within the body is 0, the amount of heat leaving the body is equal to the metabolic heat production. Conductance is then the total amount of heat leaving the surface of the animal ($M - E_{res}$) divided by the temperature gradient between the core (T_r) and the skin surface ($\bar{T}_s$)[11]. E_{res} is excluded from this heat flow, since it leaves the core directly to the environment through the respiratory tract. Conductance values reported here contain no correction for the conductance of heat by the dead body. The unit of k is W · m^{-2} °C^{-1}. Conductance is expressed in terms of surface



A plot of metabolic heat production (M) against mean skin temperature ($\bar{T}_s$) for each of 2 groups of control (saline vehicle) and 5,6-dihydroxytryptamine (5,6-DHT) treated rats over the ambient temperature range of 8–29 °C.

area, which was calculated using the relationship of 1 kg b.wt = 0.107 m^2 surface area (Lin et al., unpublished data). Measurements were made every min during the experiments, each variable being measured as a DC potential on a Hewlett-Packard digital voltmeter interfaced to an online HP9825 computer. All measurements were calculated instantaneously by the computer, displayed and printed out. At the end of the experiments, each rat was killed with an overdose of pentobarbital sodium. The head of the rat was perfused with 0.9% NaCl, followed by 10% formalin solution. Later, sections of the fixed brain were cut in 40-µm sections and stained with thionin so that the anatomical sites of the 5,6-DHT injections were verfied. The table contains a summary of thermoregulatory responses of both control and 5,6-DHT-treated rats to T_a cf 8, 15, 22 and 29 °C. The 5,6-DHT-treated animals maintained their rectal temperature within normal limits as displayed by the control animals. However, specific changes in the thermoregulatory responses were evident. The 5,6-DHT-treated rats, although showing no changes in the thermoregulatory responses at 29 °C T_a, did show a higher M and a higher k at 8, 15 and 22 °C T_a compared with saline controls. In addition, the figure compares M plotted against $\bar{T}_s$ for the 2 groups of animals. The control group exhibited a resting M of 4.0 W/kg and that below $\bar{T}_s = 35$ °C heat production

increased at the rate of 0.47 W/kg °C. Animals which received 5,6-DHT, although showing no alterations in resting M, did show a higher thermosensitivity for the increase of heat production (0.84 W/kg °C) than the saline controls. According to Baumgarten et al.[9], 5,6-DHT destroys mainly 5-HT neurons after the compound infused directly into the brain tissue. In the present study, 5,6-DHT infused directly into the POAH in a corresponding dose produced an increase in both heat production and heat loss (as indicated by changes in whole peripheral circulation) at 8, 15 and 22 °C T_a. In these amine-depleted animals, the increased peripheral circulation counteracted the increased heat production, since rectal temperature remained constant. In fact, the results are consistent with a similar work of Lin and his co-worker[5] in rabbits. At first, one might consider the possibility that the increased heat loss caused by the peripheral circulation in animals depleted of hypothalamic 5-HT elicited a compensatory increase in metabolic heat production to maintain body temperature. The ability of these depleted animals to maintain a normal body temperature in the cold in the face of increased heat loss from the body surface, by increasing their metabolic heat production, raises a problem. Since internal temperature is normal and skin temperatures are equal to, or higher than normal (table), it is apparent that the thermal drive to increase heat production does not originate from the increased heat loss. Indeed, according to a recently proposed model for the regulation of metabolic heat production, it has been shown that an increased mean skin temperature tends to suppress, rather than increase, the heat production mechanism in the central nervous system (CNS)[12]. On the other hand, a more possible explanation might be found by postulating that 5-HT depletion in the CNS may produce an increased sensitivity in the metabolic heat production to thermal input (for example, cold stimuli). Apparently, the results observed for the hypothalamic administration of 5,6-DHT in rats are rather difficult to explain in terms of the current amine theory[13,14].

1 This work was supported by grants from National Science Council of Taiwan and J. Aron Charitable Foundation (USA). The author is grateful to Dr C.Y. Chai and Mr C.C. Wei for their support.
2 A. Williams and G.P. Moberg, Comp. Biochem. Physiol. *51*, 67 (1975).
3 R.D. Myers, Brain Res. *94*, 491 (1975).
4 M.B. Waller, R.D. Myers and G.E. Martin, Neuropharmacology *15*, 61 (1976).
5 M.T. Lin, I.H. Pang, S.I. Chern and W.Y. Chia, Am. J. Physiol. *235*, R41 (1978).
6 M.T. Lin and J.T. Stitt, Physiologist, Wash. *19*, 271 (1976).
7 J. De Groot, The Rat Forebrain in Stereotaxic Coordinates. North-Holland Publ., Amsterdam 1959.
8 M.T. Lin, W.Y. Chia, C.T. Tsai and T.H. Yin, Experientia *34*, 756 (1978).
9 H.G. Baumgarten, L. Lachenmayer and H.G. Schlossberger, Z. Zellforsch. *125*, 553 (1972).
10 J.T. Stitt and J.D. Hardy, J. appl. Physiol. *31*, 48 (1971).
11 M.T. Lin, J. Pharmac. exp. Ther. *204*, 39 (1978).
12 J.T. Stitt, J.D. Hardy and J.A.J. Stolwijk, Am. J. Physiol. *227*, 622 (1974).
13 J. Bligh, W.H. Cottle and M. Maskrey, J. Physiol. *212*, 377 (1971).
14 R.F. Hellon, Pharmac. Rev. *26*, 289 (1975).

Comparison of rat, mouse, guinea-pig and human slow reacting substance of anaphylaxis (SRS-A)[1]

P. Sirois[2], D.M. Engineer, P.J. Piper and E.G. Moore

Department of Pharmacology, Royal College of Surgeons of England, London (England) and Department of Immunology, The Hospital for Sick Children, Toronto (Canada), 10 July 1978

Summary. Slow reacting substance of anaphylaxis obtained from rat, mouse, guinea-pig and human tissues have exhibited similar biological activity and have reacted in the same way to chemical and enzymatic treatments. It is concluded that they appear to be the same substance or a similar class of compounds.

The presence of a biological material released from the anaphylactic lung, different from other known mediators and producing a contraction on the guinea-pig ileum with a slow onset (SRS), was first discovered by Kellaway and Trethewie[3]. This biological entity was later called 'slow reacting substance of anaphylaxis (SRS-A)' by Brocklehurst[4]. Although a lot of effort has been put into this field during the last 40 years, the biological significance and the chemical structure of this compound is still unknown and its importance as a mediator of hypersensitivity reactions is mostly based on indirect evidence.

Many groups have investigated the release of SRS-A from different species, including rat, rabbit, monkey, human and calf[5–7]. Being part of a larger project covering some aspect of SRS-A release during anaphylaxis and its significance in acute immunological reactions, the present investigation was carried out in order to compare some pharmacological, physicochemical and biochemical properties of rat, mouse, guinea-pig and human SRS-A.

Materials and methods. 1. Preparation of SRS-A. a) Guinea-pig SRS-A was prepared from the lungs of sensitized Dunking-Hartley animals according to Engineer et al.[8,9] and charcoal extracted[9,10]. b) Rat SRS-A was prepared from the peritoneal cavity by passive sensitization as described by Orange et al.[11]. c) Mouse SRS-A was obtained from the peritoneal cells of C3H mice treated with the ionophore A-23187[12]. The crude extract was then purified by ethanol extraction and Amberlite XAD-8 chromatography[13]. Some samples have been further purified by DE-52 ion exchange and silicic acid chromatography and have migrated as rat SRS-A characteristic pattern. d) Human SRS-A has been prepared from the supernatant of passively sensitized chopped human lung as described by Sirois et al.[14]. In some experiments, human SRS-A has been prepared according to Orange et al.[15,16] and ethanol extracted only.

2. Bioassay of SRS-A. SRS-A was measured on the guinea-pig ileum according to Engineer et al.[8], or to Orange and Austen[6].

3. Drugs used. The following drugs were used: mepyramine bimaleate (Poulenc; May and Baker); hyoscine hydrobromide (BDH Chemicals Ltd); arylsulfatase type V, α-chymotrypsin, lipoxidase and atropine (Sigma Chemicals Co.); elastase (Worthington Corp. and Sigma Chemicals