Table 2. Visual experiment: average number of correct comparisons (N = 32)

Stimuli	Visual half-field right	left	t*	p
Words (max. 24)	18.4	16.7	2.65	0.01
Figures (max. 24)	19.9	20.4	0.83	0.4

*Student's t-test for paired data.

Auditory experiment. Sets of 3 digits were given as verbal stimuli. The nonverbal stimuli consisted of 5 pure tones, differing sequentially in sound frequency, which made up a characteristic form. This form had to be recognized by visual multiple choice. The duration of the sets of digits and of tones was 1.5 sec. In part 1, digits were presented to the right or left ear, simultaneously with a tonal sequence to the other ear. Parts 2 and 3 were control tasks with only digits or only tonal sequences to both ears. Table 1 shows the average number of correct responses taken from 38 righthanded students.

Significantly more digits are reported from the right ear than from the left in parts 1 and 2. Tonal sequences together with digits are equally well reported from both ears in part 1, whereas tonal sequences to both ears yield a significant left ear superiority in part 3.

Visual experiment. The verbal stimuli were common four-letter words written one above the other, and projected to one visual half-field. The words were indentical, or they differed by one letter. Pairs of nonsense figures were simultaneously presented to the other visual half-field. The figures were identical, or they differed to an extent yielding about 75% of correct responses. Pairs of identical or different words were systematically combined with pairs of identical or different figures. Stimulus duration was 80 msec. The subjects had to decide if the figures, then the words were 'same' or 'different'. The average number of correct comparisons by 32 righthanded students is shown in table 2.

Words are significantly better compared in the right than in the left visual half-field, whereas the figures are compared equally well in both half-fields.

Discussion. In agreement with previous findings, verbal stimuli are better processed by the right sensory input channels in audition and in vision as well. It makes little difference whether the verbal stimuli are presented together with other verbal, or with nonverbal stimuli. Tonal sequences are recognized differently, depending on their accompanying stimuli: Together with another tonal sequence, they are better reported from the left ear; when presented with digits, however, the ear asymmetry disappears. Similarly, the left visual half-field superiority in the perception of figures is abolished when the companion stimuli are words[12].

We conclude that the information entering the 2 sensory channels of one sense modality is not handled completely separately by the 2 cerebral hemispheres, but that there is an interaction between the 2 sides of the brain[13]. The efficiency of the left channel seems to be influenced by the type of information in the opposite channel. This influence appears to be small for the right channel. This finding can be interpreted in terms of the importance of speech in human communication. Perception and processing of speech are crucial and, therefore, they must be guaranteed. Thus we suppose that there is a cerebral mechanism able to compare and classify inputs from the sensory channels, and yielding an optimal processing of verbal and nonverbal stimuli. Additional experiments are in progress to elucidate further how and where in the brain this comparison and classification take place.

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In vivo lipolytic action of glucagon in brown adipose tissue of warm-acclimatized and cold-acclimatized rats

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Summary. Glucagon infusion caused a marked increase of brown fat venous FFA concentration, but the extent of increase was less in cold-acclimatized rats than in warm-acclimatized ones. Systemic venous FFA was not appreciably influenced by glucagon. Propanolol did not modify the changes induced by glucagon.

Ample evidence has been compiled to indicate a significant role of brown adipose tissue in cold acclimatization of various species of mammals and an enhanced activity of brown adipose tissue probably depends upon an elevated mobilization and utilization of free fatty acids (FFA) in this tissue by norepinephrine[2]. Recently, glucagon has been claimed to be a hormone of energy supply in case of exercise, fasting, etc.[3]. We have also contended that glucagon may serve an energy substrate-supplying hormone in cold acclimatization through its lipolytic action[4]. These results led us to investigate an in vivo lipolytic action of this hormone of the brown adipose tissue of cold-acclimatized as well as warm-acclimatized rats.

Materials and methods. All experiments were performed on male Wistar rats fed ad libitum under artificial light from 700 to 1900. The animals were divided into 2 groups; the one was maintained at ambient temperature of 25 °C (warm-acclimatized group) and the other at 5 °C for 2–3 weeks in the individual cages (cold-acclimatized group). The latter rats were transferred to 25 °C 18 h prior to the experiment. Glucagon (Novo Industri, A/S, Copenhagen, Denmark) was infused into the femoral vein at a rate of 2 μg/0.005 ml/min for 5 min under hexobarbital anesthesia (20 mg/100 g, intraperitoneally). Propranolol hydrochloride was injected at dosage of 500 μg/100 g intraperitoneally 10 min before the glucagon infusion. Systemic venous blood was obtained from the external

Effect of glucagon infusion (2 μg/0.005 ml min for 5 min) on the blood FFA and glucose concentrations in the external jugular and Sulzer's veins in warm-acclimatized and cold acclimatized rats

	FFA (μEq/l)		Glucose (mg/dl)	
	External jugular vein	Sulzer's vein	External jugular vein	Sulzer's vein
I. Glucagon infusion				
Warm-acclimatized rats				
Saline control (12)	364 ± 25.3	397 ± 27.7	141 ± 6.6	137 ± 4.6
Glucagon (12)	451 ± 47.8	1359 ± 86.6[c]	174 ± 4.2[c]	179 ± 4.7[c]
Cold-acclimatized rats				
Saline control (10)	308 ± 15.7	330 ± 16.4	146 ± 5.2	142 ± 6.7
Glucagon (8)	446 ± 50.4[a]	1106 ± 81.1[c]	177 ± 6.7[b]	183 ± 7.3[c]
II. Propranolol and glucagon infusion				
Warm-acclimatized rats				
Saline control (8)	346 ± 40.7	375 ± 50.4	146 ± 6.3	142 ± 5.0
Glucagon (8)	450 ± 37.2	1477 ± 84.6[c]	173 ± 5.1[b]	182 ± 6.1[c]
Cold-acclimatized rats				
Saline control (8)	313 ± 23.0	333 ± 24.9	134 ± 6.4	134 ± 5.3
Glucagon (12)	385 ± 24.0[a]	906 ± 75.3[c]	175 ± 4.2[c]	170 ± 3.7[c]

Mean ± S.E.M. Number in parenthesis indicates the number of animals. P vs Saline control rats: [a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$. Values with no marks indicate no significant difference vs Saline control rats.

jugular vein and venous blood drained through the interscapular brown fat (brown fat venous blood) from overflowed blood from both cut ends of Sulzer's vein. Whole blood FFA was measured by the method of ITAYA and UI[5] and glucose by the anthrone reagent method[6]. Statistical significance of the results was tested by Student's *t*-test.

Results and discussion. The initial body weight was 191 ± 2.2 g in warm-acclimatized rats and 199 ± 1.4 g in cold-acclimatized ones, being not significantly different between the groups. It was 264 ± 9.2 g and 234 ± 5.2 g at the experiments, respectively. The increment of body weight was significantly smaller in the cold-acclimatized rats, as previously reported[3].

In warm-acclimatized rats glucagon infusion did not modify the FFA concentration in systemic venous blood, while it caused a marked elevation of FFA concentration in brown fat venous blood (table). The glucose concentration rose similarly in both systemic and brown fat venous bloods. In cold-acclimatized rats glucagon infusion resulted in a significant but slight increase in systemic venous FFA concentration. Brown fat venous FFA concentration rose markedly by glucagon infusion, but the extent of FFA increment was significantly smaller than in warm-acclimatized rats ($p < 0.05$). Blood glucose concentration was similarly elevated by glucagon infusion in both venous bloods as in warm-acclimatized rats.

As early as 1957, DAVIDSON et al.[7] presented the first evidence of calorigenic action of glucagon. A potent in vitro lipolytic action of glucagon on white adipose tissue from rats has been consistently verified[2]. Consequently, it is quite possible that the effect of glucagon on energy metabolism is exerted through an enhanced lipolysis in addition to stimulated glycogenolysis. However, an in vivo elevating action of glucagon on blood FFA concentration was not reported until the authors observed it in the blood obtained from the tail of unanesthetized rats after a single injection of glucagon intraperitoneally[8]. Glucagon has been also found to be lipolytic in brown adipose tissue of rat when tested in vitro[9–11]. To our knowledge, an in vivo lipolytic action of glucagon on brown adipose tissue has not been reported previously. The present study apparently indicates an in vivo strong lipolytic action of glucagon on brown adipose tissue. The reason why glucagon failed to elevate the systemic blood FFA concentration remains to be explained, although some possibilities have been considered: e.g. a hyperglycemia induced by glucagon and/or insulinogenic action of glucagon[3]. A slight increase in systemic blood FFA observed in cold-acclimatized rats might reflect an enhanced sensitivity of peripheral adipose tissue to lipolytic action of this hormone in cold-acclimatization, as suggested previously[8].

It has previously been demonstrated that glucagon infusion produces the thermogenic response in the brown fat of newborn rabbits[12,13] and rats[13]. It is, therefore, conceivable that an enhanced utilization as well as release of FFA in the brown adipose tissue following glucagon serves the heat production in this tissue. PORTET et al.[14] have revealed that FFA release from the brown fat by norepinephrine infusion is less in cold-acclimatized rats, being possibly due to a greater utilization of FFA by this tissue than in warm-acclimatized rats. Moreover, the brown fat from cold-acclimatized rats accumulates more FFA in vitro in response to catecholamines, ACTH and cyclic AMP and releases lesser amount of FFA to the medium[15]. These results might explain why the extent

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of FFA release is smaller in the brown fat of cold-acclimatized rats in the present study.

With regard to the mechanism in the lipolytic action of glucagon on brown adipose tissue, SKALA et al.[16] have described that the adenylcyclase receptor for glucagon is not found in the brown adipose tissue. Brown adipose tissue is richly innervated by 2 kinds of sympathetic nerves, the one to the vessels derived from the sympathetic chain, and the other to the parenchymal tissue derived from the intrinsic ganglia[17]. Thus, it is likely that the rise in brown fat venous FFA concentration due to glucagon is secondary to a rise of catecholamine level in the brown adipose tissue as well as the circulatory blood elicited by glucagon. However, it is unlikely, since the response to glucagon was unchanged after injection of beta-receptor blocker, propranolol, which is known to suppress lipolytic as well as calorigenic action of catecholamines[18] as seen in the table. Neither calorigenesis nor increase in blood flow by glucagon is blocked by propranolol[12]. Consequently, it seems reasonable to conclude that glucagon, like catecholamines, acts directly on the brown adipose tissue in its lipolytic and calorigenic actions. The increase in blood flow through the brown adipose tissue by glucagon infusion might be partly responsible for the increased release of FFA from this tissue, although it is likely that the increase in blood flow is secondary to the metabolic action of glucagon[12]. In this connection, it is interesting to refer to the recent report suggesting that cold acclimatization results in the decreased activity of phosphodiesterase in the brown adipose tissue of rats, inducing an increased lipolysis in this tissue[19]. Thus it would appear worthwhile to investigate whether glucagon could influence phosphodiesterase activity of brown adipose tissue.

It is now widely accepted that heat production in the brown adipose tissue is governed by the sympathetic nervous system[2]. However, HULL[20] has observed that beta-blocker, pronethalol, blocked the norepinephrine-induced calorigenesis in newborn rabbits, but it did not inhibit the calorigenic response to cold. The present result, together with that of Hull'sone, seems to suggest that glucagon may act synergistically with catecholamines in determining the level of brown adipose tissue metabolic process in cold acclimatization.

The brown adipose tissue has been shown to take up glucose actively from the circulation, especially in cold-acclimatized animals[21]. However, in the present study no significant difference was observed in the elevation of blood glucose concentration between the systemic venous and brown fat venous bloods in both warm-acclimatized and cold-acclimatized animals.

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Arousal-induced increase of cortical [K^+] in unrestrained rats

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Summary. Changes of extracellular concentration of brain potassium $[K^+]_e$ were studied in lightly anesthetized unrestrained rats with ion-selective K^+-microelectrodes introduced into the cerebral cortex with a head-mounted microdrive system. Nociceptive stimuli elicited EEG arousal lasting for 47 sec on the average which was accompanied by an increase of $[K^+]_e$ from 3.0 mM to 3.31 $\pm$ 0.04 mM.

The $[K^+]$-sensitive microelectrodes[1] made it possible to examine the role of K^+-ions in various normal and pathological brain functions. The level of $[K^+]_e$ in the cerebral tissue was found to be equal to the potassium concentration in the CSF (3 mM), under resting conditions[2], and to increase to 60–80 mM during spreading depression or anoxic depolarisation[3–5] and to about 10 mM during epileptic activity[4, 6–8]. Lower $[K^+]_e$-increments were observed in the spinal cord and higher brain centres after electrical stimulation of peripheral nerves or after application of adequate sensory stimuli[9–11].

All the above studies were made in deeply anesthetized (and often curarized) animals, rigidly fixed in the head holder of the stereotaxic apparatus. Such experimental conditions preclude the use of K^+-selective electrodes for examination of $[K^+]_e$-shifts accompanying various behavioral states. The aim of the present paper was to modify the K^+-electrode technique to make it suitable for measurements in unrestrained animals by reducing the movement artefacts due to high impedance of the electrode and to changes of input-ground capacity and electrostatic induction.

K^+-microelectrodes were prepared according to the technique described by Walker[1] and modified by Vyskočil and Kříž[12]. Glass micropipettes (1.65 mm external diameter, 20 mm long, with a 5 mm long shank) contained a 0.5 M KCl solution contacting a 200 μm high column of the liquid ion exchanger (Corning Code 477317) in the siliconized tip. Their resistance was around 10^8 Ω. In order to simplify the electrode system a micropipette of the same shape but filled with 0.9% NaCl was used for field potential recording from the same region. Efficient grounding of the animal was provided by a low resistance Ag-AgCl-electrode (4 mm^2) contacting the cortical surface adjacent to the point of microelectrode insertion.

Adult hooded rats were anesthetized with urethane (0.9 g/kg) and a trephine opening 5 mm in diameter was made over the occipital cortex. The microdrive system and its fixation to the skull is shown in figure 1. 3 anchoring bolts placed around the trephine hole were used for fixation of a 3 mm high plastic ring (11) with internal diameter of 4 mm, held by 3 supporting rods (12) about 3 mm above the exposed dura (13) and bone (8). 2 silver screws (2 mm) fixed in the skull over the frontal cortex