Electrical Transcutaneous Nerve Stimulation for Relief of Itch

Transcutaneous nerve stimulation (TNS) can relieve pain (SHEALY and MAURER[1]). Itch and pain are both neuroanatomically and neurophysiologically closely related sensory modalities. The therapeutic effect of TNS on itch was therefore tested on 17 patients with various disorders and with itch as a main complaint. Stimulation was given for 1 or 2 min via electrodes placed on normal skin in the midthoracic region of the back. A pulse generator delivered pulses of 0.2 msec duration at a frequency of 60 Hz. The intensity of stimulation was slowly increased usually up to a level just below the pain threshold.

In all the patients except three the itch disappeared during stimulation. This effect continued after the cessation of stimulation. Thus the previous sometimes long-standing itch was absent for various periods of time ranging from a few hours to 1 week.

It was notable that itching was abolished all over the body, although the electrodes were regularly placed only on the back of the patient. This effect diverges from our experience of TNS for control of pain where pain relief was obtained only when painful areas or nerves supplying these areas were stimulated. The generalized abolition of itch might imply that the benefical effect is not achieved solely by mechanisms working on segmental cord levels as was originally proposed in the case of pain control (MELZACK and WALL[2]). It seems more likely that the suppressing mechanism on itch works at supraspinal levels, i.e. the brain stem, thalamus or associated limbic structures. Some patients obtained relief from itch by subliminal stimulation. This suggests that the mechanism of action may occur without the participation of systems involved in conscious sensory perception.

Regardless of the possible mechanisms at work it is a fact that 14 out of 17 patients stated that they received indisputable and considerable alleviation of itch by TNS. This is of obvious clinical importance and there are certainly also neurophysiological implications.

Résumé. La stimulation électrique transcutanée a été employée pour des patients atteints de prurigo. Dans 17 cas de personnes traitées, 14 ont été délivrées de leur mal pendant des périodes qui varièrent de quelques heures à une semaine. La base neurophysiologique de cet effet n'est pas entièrement établie.

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Relationships between Age of Submission to Environmental Stress, and Monoamine Oxidase Activity in Rats

Chronic exposure of newborn-aggregated rats to auditory, visual, and motion stimulation ('environmental stress')[1] and of adult-isolated, nonfighting rats[2], affects monoamine oxidase (MAO) activity in several organs. Moreover, it induces a faster development of receptor sensitivity to 5-hydroxytryptamine in gastric smooth muscle of newborn rats[3]. According to the concept of age-related alterations in the physiological control mechanisms of mammals, a different responsiveness of MAO to stressors, might be expected in young and old rats. The purpose of the present study was, therefore, to evaluate if MAO activity of young-adult and old rats respond differently to a prolonged stress stimulation. Brain and liver MAO were assayed, as being easily affected by stressors[1,2].

Materials and methods. Male, Charles-River rats were used; young-adults were 7 weeks of age, old rats ranged from 12 to 18 months of age. The stress used in this study was obtained through combination of flashing lights, auditory stimulation and cage oscillations, in a

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Table I. Effects of 1 week-exposure to environmental stress, on monoamine oxidase[a] activity of brain and liver in young rats

Organ	Controls	Stressed	Recovery after 7 days
Brain	1046 ± 31.9 (16)	861 ± 24.6 (8)	1001 ± 58.6 (7)
	→	$P < 0.005$[b]	n.s.
Liver	754 ± 20.6 (16)	644 ± 20.0 (8)	781 ± 24.9 (7)
	→	$P < 0.005$	n.s.

[a] Enzyme activity is expressed as μg 4-hydroxyquinoline/g protein/30 min ± S.E. No. of determinations is given in brackets. [b] The levels of significance were assessed by the COCHRAN and COX *t*-test.

randomized schedule, and was similar to a method proposed to render rats hypertensive[4-6].

All operations were carried out as described elsewhere[1]. All groups were daily subjected to 4 h of stress, 4 days per week, with an interval of 3 days until the next 4 days of stress. The stress was applied for 1 or 2 weeks on single rats; when not subjected to stressors, the animals were housed in single cages, 360 × 210 mm. At the end of the 1st or 2nd week of treatment, half of each group (the only exception being the 2 week stressed young rats), were allowed to recover for 7 days from the stress regime, and were then killed for the determinations. The other half were sacrificed between 24 and 72 h after the last stress session. The homogenation of tissues was made as previously described[7]. Monoamine oxidase activity was estimated fluorimetrically by the method of KRAJL[8], slightly modified by CENTURY and RUPP[9]. The substrate was kynuramine, converted by MAO to the fluorescent 4-hydroxyquinoline, in strong base; the plateau of the enzyme reaction was reached within 30 min. MAO specific activity was expressed as μg of 4-hydroxyquinoline formed/g protein/30 min, as the mean ± standard error. The protein content of the homogenates was determined by the micro KJELDAHL method. The differences between experimental groups were evaluated by the COCHRAN and COX *t*-test[10]. Kynuramine dihydrobromide (Sigma Chem. Co.), and 4-hydroxyquinoline trihydrate (Koch-Light Labs) were used.

Results and discussion. Table I shows that submission of young adult rats to 1 week of stress reduced MAO activity in brain and liver homogenates: the variations were of 17.8% and 14.7% respectively.

Two weeks of stress (Table II) provoked a decrease of MAO activity in both organs, by quantitatively similar effects (21.7% and 16.4% reductions in brain and liver homogenates). Unfortunately we did not examine the recovery after 7 days in this group.

Table II. Effects of 2 week-exposure to environmental stress, on monoamine oxidase[a] activity of brain and liver in young rats

Organ	Controls	Stressed
Brain	1096 ± 43.9 (8) →	858 ± 28.5 (8) $P < 0.005$[b]
Liver	803 ± 23.3 (8) →	671 ± 18.2 (8) $P < 0.005$

[a,b] See legend to Table I.

Submission of old rats to stress (Table III) decreased MAO activity in brain (16.5%) and liver (16.6%) tissues. MAO of both organs, in stressed young and old rats, returned to normal activity within the 7th day after the last stress session (Tables I and III).

From the present results, it appears that there was no apparent difference in the response of tissue MAO of young and old rats to a prolonged auditory, visual and motion stimulation. In both cases, exposure to the stress provoked a partial inhibition of brain and liver MAO: thus, the stress-provoked reduction of MAO is once more supported[1].

The complete recovery of MAO activity seen in both young and old rats supports previous findings showing that, also after a more prolonged 4 month-exposure to the stress from birth to adult age, MAO activity was normalized 10 days after the last stress[1]. We put forward the hypothesis that environmental stress might slow MAO turnover. If this is true, and in analogy with the half-times of MAO recovery evaluated after chemical inhibition with irreversible inhibitors[11-13], a still depressed activity of brain would be expected. Brain MAO, indeed, have a full recovery-time longer than 10 days, after inhibition with irreversible inhibitors. We might, therefore, consider the stress-induced inhibition of MAO rather similar to the chemical inhibition obtained in vivo by pretreating animals with *reversible* inhibitors (short-lasting effect on MAO recovery), than with irreversible inhibitors[12]. It must be underlined, however, that it is difficult to known to what extent neurogenic, stress-induced-, and chemically-provoked inhibition of MAO are similar[14,15].

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Table III. Effects of 2 week-submission to environmental stress, on monoamine oxidase[a] activity of brain and liver in old rats

Organ	Controls	Stressed	Recovery after 7 days
Brain	1039 ± 25.1 (8) →	868 ± 14.2 (8) $P < 0.001$[b]	1065 ± 27.3 (8) n.s.
Liver	645 ± 20.8 (8) →	538 ± 13.0 (8) $P < 0.005$	643 ± 13.3 (8) n.s.

[a,b] See legend to Table I.

Riassunto. L'esposizione di giovani ratti e di ratti anziani ad uno stress cronico «ambientale» (stimolazione ottica, acustica e meccanica) ha provocato una diminuzione dell'attività monoamino ossidasica (MAO) cerebrale ed epatica. L'attività MAO si è rinormalizzata entro 7 giorni dall'ultima stimolazione, sia nei ratti giovani che nei vecchi. Viene pertanto suggerita l'assenza di differenze legate all'età, nella sensibilità delle MAO a questo tipo di stress.

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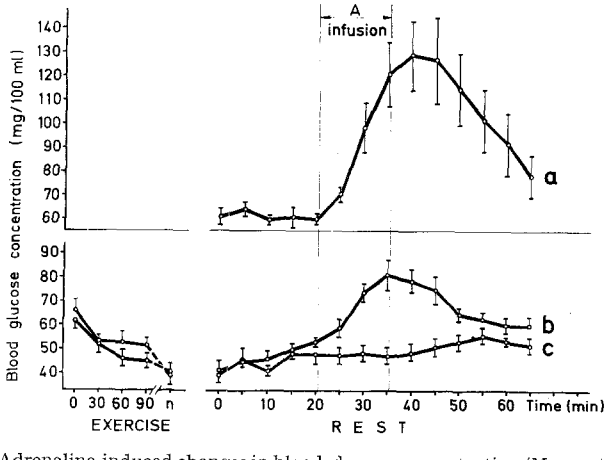
The Hyperglycemic Effect of Adrenaline Infused After Exhausting, Prolonged Physical Exercise in Dogs

During prolonged exercise, a decrease in the muscle glycogen content and blood glucose concentration have been found in dogs. Both the changes were considered as a main factor limiting physical working capacity[1]. On the other hand, a decrease in the plasma adrenaline concentration at the end of prolonged exercise was described[2]. It has not been established yet whether the exercise-induced fall in blood glucose is caused by a lower blood adrenaline concentration, an inhibition of the liver responsiveness to glycogenolytic factors, or exhaustion of the liver glycogen. In the present work, the effects of adrenaline given under control conditions, and after exhausting exercise were compared in dogs.

Materials and methods. Experiments were performed on 7 male, mongrel dogs weighing 16–19 kg, maintained on a standard, mixed diet. Before experiments the dogs were deprived of food for 18–20 h, but had free access to water. 2 main series of experiments were carried out on each dog: 1. i.v. infusion of adrenaline (adrenaline, BDH) at the rate of 2 µg/kg/min given during 15 min at rest. 2. i.v. infusion of adrenaline given at the same rate and time but 20 min after treadmill exercise performed until total exhaustion. The mean time of the run was 165 ± /SE/22 min.

Venous blood samples for glucose determinations[3] were taken at 5 min intervals for 20 min of pre-infusion rest, during the infusion and then for 25 min after its termination. Blood lactate (LA)[4], plasma free fatty acid (FFA)[5], and adrenaline (A) concentrations[6] were measured before adrenaline infusion, immediately after the infusion and 15 min later. During exercise blood glucose, LA and plasma FFA concentrations were determined every 30 min of the run. Before exercise, after its termination, and 25 min following A infusion glycogen content in the muscle samples taken from m. quadriceps femoris was measured[7]. In addition, in control experiments performed on the same dogs changes in blood glucose, plasma FFA and the muscle glycogen content were followed during 65 min after termination of exercise without A infusion.



Adrenaline-induced changes in blood glucose concentration (Means ± SE). a) A infusion without previous exercise; b) A infusion after exercise; c) controls without A infusion.

Results. During exercise blood glucose level decreased by 20.3 ±/SE/2.6 mg/100 ml ($p < 0.001$). The hyperglycemic effect of A infused under control resting conditions was markedly higher than that after the exhausting exercise (Figure). The maximal increase of blood glucose in resting dogs was 75.6 ± 13.8 mg/100 ml, while after exercise it amounted only to 30.7 ± 5.2 mg/100 ml. In most cases the peak values of blood glucose concentrations were attained in 5 min after the end of infusion in the 1st series, and at the end of infusion in the 2nd series. The differences between adrenaline-induced increases in blood glucose concentration in the 1st and 2nd series were statistically significant from the 10th min of infusion to the 15th min after its termination ($p < 0.001$). Without A infusion, blood glucose concentration slowly increased during 65 min of the psot-exercise period (lower part of the Figure).

The muscle glycogen content decreased during exercise from 1.012 ± 0.033 to 0.168 ± 0.061 g/100 g of the tissue ($p < 0.001$) and was maintained at the low level at 65 min of the post-exercise period both with and without A infusion. Adrenaline infused in resting dogs (series 1) caused higher increases in the plasma FFA (from 466 ± 15.9 to 707 ± 42.2 µEq/l) than after exercise (series 2) when it rose from 781 ± 60.0 to 911.6 ± 78.1 µEq/l, but the difference between the two series was not statistically significant ($p > 0.05$). The exercise by itself caused a marked increase in the plasma FFA level from 499.0 ± 15.0 to 816.0 ± 35.0 µEq/l ($p < 0.001$). Without A infusion, the plasma FFA was maintained at the post-exercise level during 65 min of the recovery period.

The infusion of A induced similar increase of blood LA in both series of experiments (by 0.9 ± 0.26 mM/l in the 1st and by 0.9 ± 0.43 mM/l in the 2nd series). At the end of exercise, blood LA reached the level of 2.61 ± 0.22 mM/l, which was by 0.68 ± 0.20 mM/l higher than that before the exercise.

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