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Effect of repeated electroconvulsive shock on plasma noradrenaline and adrenaline in man

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Summary. The concentration of noradrenaline (NA) and of adrenaline (A) in plasma was measured before and 3, 30 and 60 min after single and repeated electroconvulsive shocks (ECS). Single ECS resulted in an activation of the sympatho-adrenal medullary system; however, after the treatment had been repeated 4 times there was evidence of a diminished response of the peripheral sympathetic nervous system in comparison to the response to the first ECS.

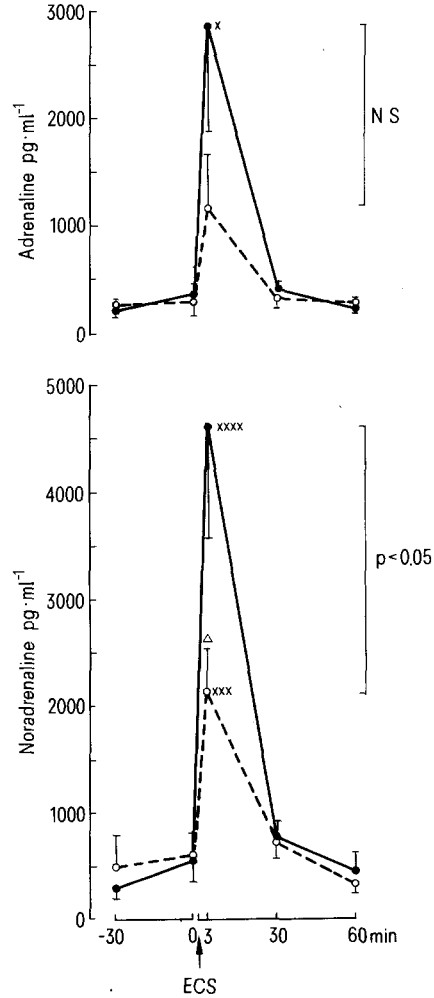
Electroconvulsive shock has been shown to affect several biochemical parameters of the central noradrenergic system in the rat. It increases the activity of tyrosine hydroxylase[1] and the turnover and release of NA[2], and decreases the high affinity uptake of NA into synaptosomes[3]. Moreover, the sympatho-adrenal medullary activity of rats exposed to footshock was also found to be increased[4].

In the present study, we have examined the sympathoadrenal medullary response of man (psychiatric patients) to single and repeated ECS.

Materials and methods. The experiments were performed at the Regional Mental Hospital in Pezinok, with psychiatric patients for whom ECS without anticonvulsive premedication (ACP) was indicated for psychiatric reasons as a routine procedure. The study included 5 males, ranging in age from 26 to 52 years, with body weights within the normal range. 4 patients were diagnosed as schizophrenic and 1 as endogenously depressive. All patients were receiving antipsychotic drugs (chlorpromazin, chlorprothixen or clozapin) which had been omitted only on the day of ECS. During the last 6 months before our investigation the patients had not been subjected to ECS. After overnight fasting ECS was applied between 7.30 and 8.30 h by bitemporal electrodes (400–500 mA at 120 V during 0.9–1.1 sec). Special care was taken to prevent injury during convulsions. Venous blood samples were taken 30 and 0 min before ECS and 3–5, 30 and 60 min after the ECS, both during the first and the 4th ECS. In all cases the 4 ECS were applied during a 8-day period. A modification of a sensitive radioenzymatic assay was used to measure plasma NA and A[5,6]. Student's t-test for unpaired values and analysis of variance were used to determine the statistical significance. Results are given as means ± SEM.

Results and discussion. Values for NA and A are depicted in the figure. Immediately after the first ECS, NA peaked up to a level of about 4600 pg/ml. The 4th repetition of ECS was, however, connected with a significant diminution ($p < 0.05$) of the NA response which still was increased significantly ($p < 0.01$). On the other hand, although the plasma A response to the 4th ECS was not statistically significant compared to the preshock level, no significant difference between plasma A levels during the 1st and 4th ECS could be registered. All statistical calculations made by Student's t-test were confirmed by the analysis of variance.

Exposure of psychiatric patients to an intensive stress stimulus (i.e. ECS without ACP) resulted in an activation of the sympatho-adrenal medullary system as evidenced by striking increments in circulating levels of NA and A. A similar finding has been described earlier in the rat[4]. However, it should be mentioned that no activation of the sympathetic nervous system after ECS with ACP was



Pattern of plasma NA and A response to the 1st and the 4th electroconvulsive shock in 5 psychiatric patients. Statistical significances to preshock values are indicated by asterisks. x, xxx and xxxx belong to $p < 0.05$, 0.01 and 0.002, respectively. $\Delta = p < 0.05$ compared to 1st exposure.

observed as evaluated by the serum dopamine-beta-hydroxylase activity in man[7]. Nevertheless, the serum level of this enzyme has not been generally accepted as a measure of the peripheral sympathetic activity.

Experiments with repeated ECS show an evidence of diminished response of the peripheral sympathetic nervous system to repetition of ECS in man, but some other factors (degradation and/or depletion of catecholamines) or a specific reaction in schizophrenia could not be excluded.

It is interesting that with as few as 4 exposured to ECS the response of the sympatho-adrenal medullary system to such an intensive stimulus was diminished. In animal experiments a diminished response of plasma catecholamines to repeated immobilization was observed in blood collected by chronically indwelling catheters[8] but in rats that had been decapitated[9], which represented a new stimulus for the animals, a significant increase of plasma catecholamines was found. The capacity of the adrenal medulla of repeatedly stressed rats is greatly increased[10] but plasma catecholamine levels are reduced suggesting that the adaptation to a given stimulus is not a question of the adrenal medullary responsiveness but might be mediated by a decreased brain or spinal cord activity. Moreover, ECS might also be expected to increase the availability of NA at the synapse and could initiate a neurochemical adaptation at the receptor level[11].

On the basis of our experimental data a statement could be made that repeated ECS induces a decrease in plasma catecholamine response in man. The mechanism of this adaptation is not clear yet.

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Molting processes and hormonal control: an in vitro model

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Summary. In vitro cuticular deposition by larval epidermic material depends on hormonal conditions. Quantitative and qualitative variations are reported according to defined stimulations. Possible specific actions of each hormone are discussed.

We have investigated the in vitro development of the abdominal integument of the 4th larval instar of the locust *Schistocerca gregaria.* 3 principal events occur under our experimental conditions[1-3]: 1. cuticular deposition, 2. cellular alterations, 3. cellular differentiation. This paper summarizes the different secretory activities and the intensity of cellular alterations obtained with epidermic material under defined hormonal conditions.

Material and methods. Abdominal explants are excised aseptically and cultured in a hormone-free medium[4] or in medium with synthetic hormones (alpha and betaecdysone, juvenile hormones (C 18 JH 1, C 17 JH 2 and C 16 JH 3). Co-cultures of integument and endocrine glands (prothoracic glands and corpora allata) are also performed. All the experiments including. JHs are performed in vessels coated with 1% siliclad to avoid adsorption on the walls. The explants are cultured for a week and then fixed for ultrastructural study.

Results and discussion. Cultures in a hormone-free medium (figure 1). In a hormone-free medium[1,5], after a critical period (CP) 2 types of cuticular secretion are displayed. This CP lasts until between the 4th and the 5th of the 7 days of the 4th larval instar. Before the end of this CP, epidermic cells deposit a procuticular material but never new epicuticle that would prove that a new cuticular cycle has started. If cells adhere to the old cuticle, the material proves to have a lamellar organization; otherwise, it becomes less abundant and cells deposit a fibrillary material which is randomly disposed. These results are in accordance with those of Miciarelli et al.[6]. Every alteration produced by hormonal stimulation is determined after comparison with a 2-day-old explant which is considered as a control.

Actions of synthetic ecdysteroids. Alpha and bete-ecdysone have been applied in concentrations increasing from 0.001 to 15 µg/ml[7]. With such stimulation the epidermis can overcome the CP and deposit a new cuticle composed of epicuticular layers and under-lying procuticular material. In the constant experimental time of a week, the different secretory events and alteration intensities are shown in figure 2. With alpha ecdysone, alterations are already at a maximum with 0.001 µg/ml and remain in such a state as the dose increases. The CP is overcome with doses of 2–5 µg/ml. With beta ecdysone, partial alterations take place with doses from 0.001 to 0.5 µg/ml and decrease as doses increase. The CP is overcome with only 0.1–0.5 µg/ml. With doses above 1 µg/ml the CP is repeatedly overcome and the epidermis deposits several cuticles.

At physiological concentrations, alpha ecdysone is particularly effective in inducing the preparatory processes of molting. Beta ecdysone displays a qualitatively similar but slower and less active response. In addition, beta ecdysone increases the quantity of secreted material and allows the epidermis to initiate a new cuticular secretion cycle. Such events are not noticed with alpha ecdysone.

Actions of juvenile hormones (C 18 JH 1, C 17 JH 2 and C 18 JH 3). The range of concentrations studied is 0.001–0.100 µg/ml. Doses above 0.100 µg/ml provoke an immediate destruction of cells. JH 2 and JH 3 have an inhibitory effect on cuticular deposition and on the processes of cellular alteration. Contrary to this, JH 1 mainly stimulates the procuticular secretion activity at a dose of 0.050 µg/ml. At the same time, significant detachments occur and the epidermis shows the same alterations as in a pre-apolysis stage in vivo.