mals[27-29]. The pathological findings in all these studies are not specific and have also been observed in myocardial ischemia[30] as well as in deficiency in magnesium[31] and potassium[32]. Nevertheless, in view of our present results it can be speculated that continued exposure to high levels of norepinephrine might play a role in the development of cardiomyopathy in chronic alcoholism due to interference with both cardiac contractility and metabolism.

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Habituation to Iterative Photostimulation in the Palmar Skin Conductance Response of Mice, its Delay by Psychoanaleptics

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Summary. In mice, iterative photostimulation results in habituation, detected in the palmar skin conductance response. Psychoanaleptics delay this habituation in proportion to the dose administered.

On human subjects, it has been demonstrated[1] that repetition of stimuli produces decrements in the magnitude of the skin conductance response (SCR). Habituation has been detected in mice, where iterative photostimulation (IPS) provoked first a progressive decrease of the amplitude of the palmar SCR (PSCR), then its annulation[2]. This phenomenon – iterative photostimulation habituation (IPSH) – is delayed by psychoanaleptics[2,3].

Methods. Swiss Orl male mice (body weight 18 to 25 g) were randomized into batches of 10. The animals were vertically restrained in individual wire cylinders (diameter 2.5 cm, height 7.5 cm). A 100 W glow lamp located 10 cm above their heads was automatically switched on for 7 sec every 2 min (photostimulus: PS). The PSCR was recorded as the mice grasped by reflex the electrodes of a palmar skin conductance-meter which has been described elsewhere[4]. Following a scheme previously used for studying its magnitude[5], PSCR was recorded every 10 min and the amplitude calculated in relation to the corresponding initial reading.

Drugs were given i.p. or p.o. between the 1st and the 2nd PS. Each batch of mice was dosed in such a way as to achieve logarithmic increase of dosage over the whole experiment.

Results. Regression equations 'delay of habituation (1/100 h)/log dose (mg/kg)' in the Figure clearly show the delaying effects on IPSH of the psychostimulants tested: amphetamine sulf., dexamphetamine tart., caffeine and pyrisuccideanol dimal.

Discussion. Together with other autonomic and EEG responses, SCR is a part of the orienting reflex[6]. It readily habituates upon repetition of the stimuli. This phenomenon could occur in the visual pathways and

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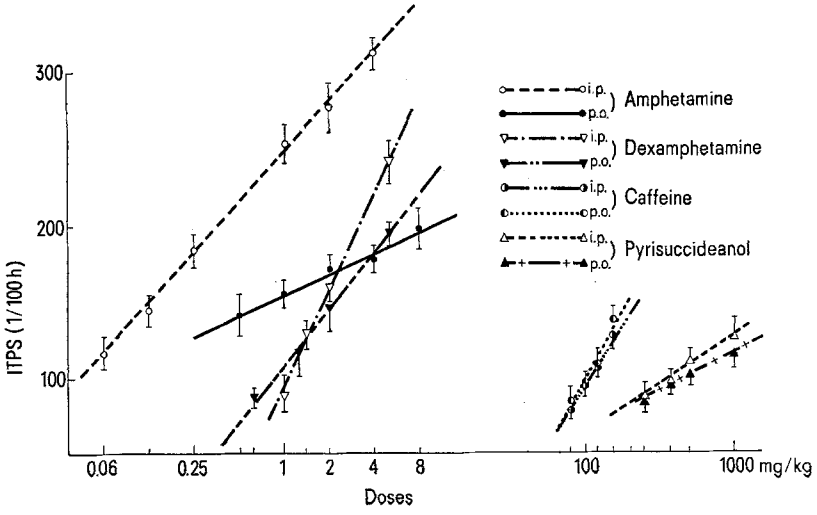

Dose-related inhibition by psychoanaleptics of habituation to iterative photostimulation in the palmar skin conductance response of mice.

cortex[7] but the reticular activating system (RAS) must intervene greatly because higher levels of attention are associated with large-amplitude SCRs[6] and also because SCR itself is obtained by stimulation of RAS[8]. IPSH could therefore be considered as an index of the level of behaviour arousal during monotonous sollicitation.

In the present method, amphetamine sulf. (i.p.) is significantly active even at such a low dose as 0.06 mg/kg, while 5 mg/kg are necessary to increase locomotor activity (LA). Similarly pyrisuccideanol dimal. delays habituation at doses between 0.250 and 1 g/kg – a range where no LA increase is to be seen.

The IPSH-method is therefore more sensitive than LA-tests as far as the drugs used are concerned. In addition, it must be pointed out that the sought-after medical effect of psychoanaleptics is the maintenance of high arousal and attention capacity rather than muscular hyperactivity. Thus, even though species differ in response, the IPSH-test probably has a more predictable value than LA-tests in the search for psychoanaleptics. Moreover, contrary to EEG-tests, IPSH-test needs no special preparation and allows systematic studies on numerous batches of animals. Finally, habituation is, with sensitization, one of the most elementary forms of behavioral plasticity[9] and may also be considered as a special kind of conditioning[10]. The IPSH-test has thus proved itself a useful tool in psychopharmacological research.

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Antifibrinolytic Properties of Oxyphenbutazone in vitro

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Summary. The authors found that oxyphenbutazone (Tanderil®) added to culture medium, in amounts giving a final concentration of 10–100 μg/ml, causes a decrease in the liberation of fibrinolytic agents from explants of various tissues cultured in vitro.

The demonstration of fibrinolytic activity in tissue cultures in the early thirties prompted the first studies on tissue fibrinolysis (Fischer[1]; Santesson[2]). In recent years attention has again been focused on the fibrinolytic properties of tissue cultures (Bernik and Kwaan[3]; Åstedt and Pandolfi[4]; Åstedt et al.[5]) in an endeavour to find a model for studying the synthesis of fibrinolytic enzymes in the tissues and the mechanism of liberation of these agents from the cells. A method has recently been devised in which organ explants are cultured in the presence of standardized clots (Åstedt et al.[6] 1971). The advantage of this method is that fibrinolytic activators can exert their effect as soon as they are released into the medium, i.e. before they are inactivated (Åstedt and Pandolfi[4]). The amount of fibrinolytic agents released is indirectly assessed by immunochemically assaying the fibrin degradation products (FDP) accumulated in the culture medium. This method is a good experimental model for studying the mechanism of release of fibrinolytic activators from cells. Information on this phenomenon is valuable since cumulative evidence indicates that liberation of fibrinolytic agents from the active structures of tissues plays a role in the pathogenesis of thrombosis (Nilson and Isacson[7]), in inflammation (Donaldson[8] 1970) and in tissue repair processes (Astrup[9]).

This paper is a preliminary report on the depressive effect of an anti-inflammatory substance, oxyphenbutazone (Tanderil®) on the fibrinolytic activity of tissue cultures.

Material and method. Kidneys were obtained from newborn albino rats. In one case an extirpated cancer of the ovary served as donor material. The tissue fragments were washed in Parker 199 culture medium (SBL, Stockholm, Sweden) and divided into pieces about 1 mm across. These explants were then placed on slices of gel foam (Spongostan, Ferrosan, Malmö, Sweden), as a rule 3 explants per slice. The slices of gel foam with the explants were transferred to Leighton tubes (2 slices in each tube) containing Parker 199 (1.5 ml as a rule) culture medium. A 4 cm long glass tube (outer diam. 3 mm, inner 1.5 mm) open at one end was then inserted into the Leighton tube. This tube was filled with a mixture of 1 ml human plasminogen-rich fibrinogen (Kabi, dissolved in distilled water) and a minimal amount of bovine thrombin (Topostasin Roche, 7.5 NIH U/ml 0.15 *M* NaCl) resulting in a cylinder of fibrin occupying the cavity of the tube. In one experiment a 1 ml standard human fibrin clot at the end of the Leighton tube was used as substrate (Åstedt et al.[6]).

During culture of active tissues, the fibrin cylinder dissolved progressively from the open end of the glass tube. At certain intervals (12 or 24 h) 0.06 ml of the culture medium was collected and examined immunochemically for FDP (Niléhn[10]). Oxyphenbutazone was added to the

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