ing to the results obtained, the type of opium examined shows on ageing a marked tendency towards increasing the yellow colour of the extract.

The nature of the water-soluble yellow pigments, which occur rather abundantly especially in old opium, does not seem to have been studied in detail so far. In order to explain the formation of the yellow pigment during the storage of opium, the intensity of the colour of a number of extracts belonging to different opium types has been compared with the results of the corresponding samples, obtained by means of our method of direct ultraviolet absorption spectrophotometry[1]. It has been observed that the intensely coloured samples of several types of opium were particularly distinguished by a high ratio E_{280}/E_{290}, obtained by our first extraction procedure, whereas most of the samples having only slightly coloured extracts exhibited rather low values of the same extinction ratio. As previously stated[1], this ratio is mainly affected by the quantity of meconic acid, being in reverse relation with the content of this constituent in opium. Consequently, a decreased content of meconic acid could be considered in general to be a characteristic of intensely coloured extracts of old opium.

In our opinion, an increased quantity of yellow pigments might be related to some extent to the parallel decrease of the meconic acid content in opium after longer storage. At present, we are not able to explain in detail the possible participation of the meconic acid molecule in the process of forming the yellow pigments. However, the γ-pyrone ring of meconic acid could possibly be considered as a component of the structure of a number of widely distributed natural pigments of the flavone group. As is known, the formation of these pigments in plants has not been explained so far in a satisfactory way.

It is obvious that various conditions of storage of opium (temperature, light, humidity) will affect to a certain degree the formation of the yellow colour observed. However, it should be mentioned that only slight differences in colour have been found between the extracts prepared from the surface and those from the inner part of the old opium cakes examined, which were exposed to light for more than 30 years.

Some preliminary examinations have shown that the age of some other types of opium (Iranian, Turkish) could also be established in a similar way. However, it is to be expected that various types of opium would give rather different results due to the differences in their content of meconic acid and other organic constituents. Therefore, such age determinations should be considered as reliable only if performed with opium of known origin, by means of a procedure tested and found suitable for the type concerned.

The procedure used in this paper is to be regarded as a preliminary one, even if applied only to the Macedonian opium. By calculating the results on a dry basis and by using a better method for the extraction (in order to avoid the absorption of pigments on the insoluble substances), one will undoubtedly obtain more exact and reliable results.

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Institute for the Control of Drugs, Zagreb (Yugoslavia), January 28, 1959.

Résumé

L'intensité de la coloration jaune des extraits aqueux tamponnés d'opium macédonien est directement liée à l'âge de l'opium, ce qui permet d'évaluer approximativement l'année de la production de cet opium par un procédé colorimétrique très simple. L'accroissement de la teneur en pigments jaunes semble être accompagné d'une diminution parallèle de l'acide méconique au cours du vieillissement de l'opium.

Noise Induced Convulsions in Mice

In the past two decades considerable effort has been expended in attempts to define the physiological and/or psychological basis underlying audiogenic seizure susceptibility in animals. Much of the earlier literature through 1946 has been reviewed by FINGER[1]. Recently, BEVAN[2] has reviewed research from 1947 to 1954.

During the course of our studies on noise stress effects in animals[3] it was repeatedly observed that mice which were presumed seizure-resistant would enter into a violent running phase followed by a clonic or clonic-tonic convulsion when exposed to high intensity noise. This occurred more frequently with intense high frequency noise exposure than with intense low frequency noise. Despite the fact that there is no satisfactory explanation of the seizure triggering mechanism, a number of investigators adhere to a hypothesis advanced by MORGAN *et al.*[4] which maintains that the convulsion is the result of excessive auditory stimulation which effects overexcitation of auditory centers with a resultant spread into adjacent motor centers. Such an interpretation implies that the audiogenic-seizure may be a normal physiological response to a sound stimulus which exceeds the sensory threshold of the auditory center. If one accepts the possibility that sound induced convulsions are not a manifestation of some inherent physiological defect, it should be possible to use this abnormal behavior response as an endpoint for assessing an animal's limits of auditory sensitivity. It is with this in mind that the present study was initiated.

The animals used came from two laboratory strains of mongrel Swiss albino mice originally developed by FRINGS *et al.*[5]: one showing a high incidence of convulsions when exposed to noise (110 db, 10–20 kc) but no fatalities, and the other showing no convulsive response to noise. In the present investigation only the latter (seizure-resistant) mice were used.

Mice were selected at random from laboratory cages and exposed to one of three noise situations: (a) noise of moderate intensity in the high frequency range (110 db, 10–20 kc), (b) intense low frequency noise (135 db, 300–4800 cps), and (c) intense high frequency noise (132 db, 2–40 kc). Each mouse was exposed once for a duration of 1 min and the behavioral responses recorded especially with respect to the type of seizure elicited, i.e. running, clonic, or clonic-tonic.

[1] F. W. FINGER, Psychol. Bull. *44*, 201 (1947).

[2] W. BEVAN, Psychol. Bull. *42*, 473 (1955).

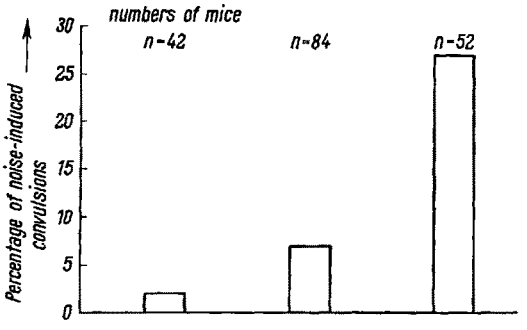
[3] These studies were aided in part by the Aero Medical Laboratory, Wright Air Development Center, Wright-Patterson Air Force Base under contract AF 33(616)-2505. This is paper No. 2349 in the Journal Series of the Pennsylvania Agricultural Experiment Station.

[4] C. T. MORGAN and H. WALDMAN, J. Comp. Psychol. *31*, 1 (1941).

[5] H. FRINGS and M. FRINGS, Behavior *5*, 305 (1955).

It was found that only one of 42 mice exposed to moderately intense high frequency noise experienced a violent running type seizure. This was not followed by a clonic or clonic-tonic convulsion. Of the mice that were exposed to intense noise at relatively low frequencies six out of 84 mice experienced seizures. This increase is not statistically significant indicating that the acoustic pressure level is not as important as the frequency with respect to seizure induction. With intense high frequency noise 14 of 52 mice went into seizures. This increase in the incidence of convulsions is significant at the 0·01% level of confidence using the chi square test. It was further noticed that only with intense high frequency noise was the running phase characteristically followed by a clonic or clonic-tonic convulsion.

These results are graphically summarized in the Figure where the incidence of convulsions (irrespective of the type) is expressed in %.



Incidence of convulsions in a 'seizure resistant' mouse strain exposed to three different noise situations.

One may conclude from these data that the threshold for seizure induction by noise appears to be lower at high frequencies. This is in agreement with reports that the optimum auditory sensitivity of laboratory rodents lies somewhere between 12–25 kc[6]. It further emphasizes the need for the accurate specification of the intensity and frequency of the sound stimulus in studies which involve the use of so called seizure susceptible and seizure resistant mouse strains.

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Zusammenfassung

Es wird die Anzahl der Krampfanfälle bestimmt, die durch intensiven niederfrequenten (135 db, 300–4800 Hz) und hochfrequenten (132 db, 2–40 kHz) Schall bei Mäusen ausgelöst werden. Die Krampfschwelle ist bei hohen Frequenzen wesentlich geringer als bei niedrigen. Dieses Ergebnis stimmt mit Berichten, dass die optimale Sensitivität von Nagetieren bei 12–25 kHz liegt, überein.

[6] H. Frings and M. Frings, J. Acoust. Soc. Amer. *24*, 163 (1952).

Action de la Psilocybine sur le cerveau du lapin

Le principe actif du champignon hallucinogène *Psilocybe mexicana* Heim a été isolé sous forme cristalline sous le nom de Psilocybine et identifié comme étant un dérivé indolique phosphoré, susceptible de produire les mêmes effets psychotropes chez l'homme que le champignon lui-même[1,2]. Il présente sur l'organe isolé un faible antagonisme à l'égard de la Sérotonine. Chez le lapin éveillé, il produit (1–3 mg/kg par injection intraveineuse) une mydriase, tachycardie, tachypnée, élévation de la température et même de la glycémie. Le comportement somatique présente peu de signes d'excitation, voire même une certaine tranquillité. L'activité électrique cérébrale du lapin curarisé montre un syndrome d'éveil, avec disparition des spindles et des ondes lentes. Chez le chat, les réflexes spinaux sont le plus souvent augmentés[3]. Nous avons jugé intéressant de compléter nos investigations sur les stimulants centraux par une analyse électrophysiologique de l'action de ce dérivé indolique, qui après déphosphorylisation, s'est avéré être une 4-hydroxy-diméthyl-tryptamine[4].

Méthode. La Psilocybine a été injectée au lapin éveillé aux doses de 1,5, 2, 2,25 et 5 mg/kg intraveineuses (lapins Nos 425, 427, 445, 451, 452, 454, 456). On a observé simultanément le comportement viscéral et somatique, ainsi que l'activité électrique du cerveau intact ou décérébré (cerveau isolé). L'action de la stimulation électrique de la formation réticulée mésencéphalique, du thalamus médian et latéral, de l'hippocampe dorsal sur l'activité du néocortex, du paléocortex hippocampique et du mésodiencéphale a été enregistrée avant et après la drogue. La documentation EEG a été complétée par une analyse oscillographique des potentiels évoqués.

Résultats. Dans la sphère végétative, on observe une mydriase, une élévation prolongée de la pression artérielle (10 mm Hg après 5 mg/kg), une bradycardie transitoire et une hyperpnée prolongée. Le comportement somatique se caractérise à la fois par une certaine tranquillité et par une légère hyperexcitabilité aux stimuli extérieurs (mâchonnements, secousses musculaires, agitation épisodique).

L'EEG montre un syndrome d'éveil complet, avec désynchronisation du néocortex moteur et somesthésique, disparition des spindles et des ondes lentes, en même temps qu'une synchronisation du paléocortex hippocampique, du noyau caudé, du thalamus, voire même de la formation réticulée mésencéphalique et du cortex visuel (Fig. 1*a*, *b*). Ce syndrome d'éveil débute peu après l'injection; il atteint un maximum entre 30 et 90 min. Dans l'hippocampe et le thalamus, les activités synchronisées alternent parfois avec des activités moins synchronisées ou même désynchronisées. Après décérébration intercolliculaire, l'injection intraveineuse de Psilocybine (2 mg/kg) développe encore un faible syndrome d'éveil: désynchronisation du néocortex, raccourcissement des spindles, synchronisation fugace de l'hippocampe et du thalamus (Fig. 1*c*).

Les potentiels évoqués dans le cortex somesthésique par stimulation d'un système afférent spécifique (Noyau

[1] A. Hofmann, R. Heim, A. Brack et H. Kobel, Exper. *14*, 107 (1958).

[2] A. Hofmann, A. Frey, H. Ott, Th. Petrzilka et F. Troxler, Exper. *14*, 397 (1958).

[3] H. Weidmann, M. Taeschler et H. Konzett, Exper. *14*, 378 (1958).

[4] A. Hofmann et F. Troxler, Exper. *15*, 101 (1959).