conditions indiquées. Disposant ainsi de méthodes permettant d'individualiser avec sécurité, par chromatographie sur papier mono- et bidimensionnelle, un ensemble d'iodothyronines, nous avons entrepris des recherches pour caractériser certaines de celles-ci dans la glande ou dans le plasma sanguin par radiochromatographie[3].

Des lots de rats ♂ de 150 g environ, recevant par voie intrapéritonéale de 50 à 75 μc ^{131}I (^{131}I Na sans entraîneur), ont été sacrifiés 12, 24 ou 48 heures après et nous avons recherché la 3:3'-diiodothyronine et la 3:3':5'-triiodothyronine dans l'hydrolysat enzymatique de leur corps thyroïde (protéinases pancréatiques totales et papaïne) et dans leur sérum sanguin. La 3:3'-diiodothyronine a été mise en évidence dans l'un et l'autre 12 heures après l'injection d'iodures marqués, par autographie et par mesure directe de la radioactivité des chromatogrammes mono- et bidimensionnels obtenus avec les solvants indiqués plus haut. Son taux est de l'ordre de 10 à 25% de celui de la thyroxine. La 3:3':5'-triiodothyronine a été identifiée par les mêmes méthodes dans l'hydrolysat enzymatique du corps thyroïde, lequel en renferme des quantités beaucoup moindres que celles du dérivé diiodé. Ni l'un ni l'autre de ces constituants nouveaux de la thyroglobuline ne sont désiodés par la déshalogénase de la glande; ils sont donc sécrétés par celle-ci. Ainsi s'explique la présence dans le sérum de la 3:3'-diiodothyronine qu'accompagne sans doute des traces de son homologue 3:3':5'-triiodé.

L'activité antigoïtrogène de la L-3:3'-diiodothyronine pure est égale à 85% de celle de la L-thyroxine, ce qui permet de considérer la première comme une nouvelle hormone thyroïdienne jouant un rôle physiologique important. La L-3:3':5'-triiodothyronine ne présente qu'une activité antigoïtrogène minime de l'ordre de 10% de celle de la L-thyroxine, mais elle peut n'être pas dépourvue d'autres propriétés du type thyroxinien.

La sécrétion hormonale du corps thyroïde renferme au moins quatre dérivés iodés de la thyronine, probablement tous de la série L: la thyroxine, la 3:5:3'-triiodothyronine, la 3:3':5'-triiodothyronine et la 3:3'-diiodothyronine. La multiplicité de ses constituants évoque celle des produits de la sécrétion d'autres glandes endocrines; il convient de rechercher dans quelle mesure chacune des quatre hormones connues exerce une action préférentielle vis-à-vis de l'un ou de l'autre de ses récepteurs.

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Reçu le 10 juin 1955

Cholinesterase content and functional activity in the central nervous system

The correlation of behavior in animals with their brain enzyme activity is an important approach to the study of neurological and mental illness[1,2]. An experimentally controlled behavioral pattern may be produced in rabbits[3] by the unilateral intracarotid injection of an anticholinesterase drug, di*iso*propylfluorophosphate (DFP). Such a pattern is manifested by the rabbits continuous compulsive circling. It is postulated in the present report that the level of cholinesterase activity in the cerebral cortex of these animals is directly correlated with the functional state of the nerve tissue. This tissue may function in one of three possible states: (1) unaffected, *i.e.* within the range of physiological safety, (2) stimulated or (3) inhibited. Evidence for these states is inferred from a correlation of the animals behavior with the ChE activity in their right and left cerebral cortices. It should be further noted that extirpation of specific areas of the cerebral cortex evokes compulsive turning toward the injured side, whereas stimulation of these areas will produce movements of the head and eyes away from the stimulated side[4]. Therefore the conclusions to be presented are in agreement with previous work which has implicated the cerebral cortex in the production of forced turning movements[4].

DFP (0.05, 0.10 or 0.15 mg/kg) was injected into the right common carotid artery which irrigates chiefly the right side of the brain. Within a few minutes most of the rabbits exhibit compulsory turning movements away from the side of the DFP injection ("lefters"); they may continue this abnormal postural pattern for several hours. A few animals circle toward the side of the DFP injection ("righters"), whereas some of the observed rabbits show no change in their normal mode of progression ("neutrals"). All of the circling rabbits exhibit an asymmetry in their brain ChE pattern; the enzyme activity is much lower on the side of the DFP injection. On the other hand, no asymmetry in the ChE pattern is noted in the rabbits which do not circle.

Although many brain areas in our preparation have been analyzed for their ChE activity only the biochemical lesions of the cerebral cortex appear to be essential for the production of compulsive circling. The neurohormone, acetylcholine (ACh), accumulates when ChE is inhibited[5,6] and it is this agent which is thought to produce the observed effects. However, only the ChE data are available at this time and the correlation of the functional states is made with the enzyme activity alone and not with the neurohormone upon which it acts.

The ChE data for the left and right cerebral cortices of circling rabbits is presented in Fig. 1. The left cortex of animals which circle toward the left is relatively unaffected and even with large doses of DFP it never falls below 50% of normal. It is postulated that this is the zone of physiological safety and the function of the tissue is unaffected by the partial inhibition of the ChE. On the other hand, the enzymic activity of the right cortices of these animals varies between 29 and 42% of normal. It is suggested that such a reduction in ChE activity results in the stimulation of this tissue (Curve B) and thereby produces circling toward the opposite side. This hypothesis is further supported by the data presented in the figure for the left cortex of animals that turn toward the right (Curve B). The enzymic activity in this tissue is quite similar to that of the opposite cortex in the "lefters". The left cortex in "righters" is presumably stimulated thereby producing rabbits which circle toward their right side. Thus in both instances the concentration of ChE between 25 and 50% of normal appears to be the level at which stimulation of the cortical tissues occur.

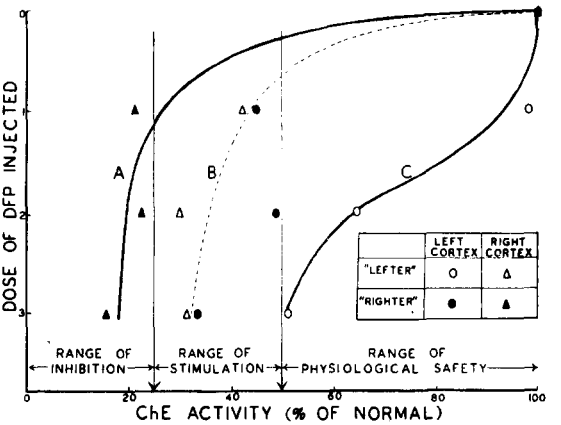

Fig. 1. The cholinesterase data for the left and right cortices of circling rabbits. The animals exhibited compulsive circling movements as a result of the intracarotid injection of DFP. A single dose of DFP is 0.05 mg/kg. The control values were obtained by the substitution of water for the DFP. Each point represents the mean ChE value for at least 7 animals.

The effect of the reduction of ChE activity below 25% of normal observed in the right cortex of "righters" may cause an inhibition of neuronal function. This conclusion is warranted if conduction in the central nervous system can be compared to that in peripheral nerve in which case it has been shown[7,8] that a reduction in ChE activity as low as that of the right cortex in our preparation will block axonal conduction. Therefore, the ChE level found under these conditions is associated with an inhibition of cortical tissue function (Curve A). The inhibition of the right cortex at the same time that the left cortex is being stimulated results in the production of a rabbit which circles compulsively toward its right side.

In conclusion it has been postulated that three functional levels of activity in the cerebral cortex can be associated with three distinct ranges of its ChE content: (1) the range of physiological safety occurs when the enzyme activity is between 50–100% of normal, (2) the range of stimulation is between 25 and 50% of normal, and (3) the range of inhibition is correlated with a fall in ChE activity below 25% of normal. Furthermore, these ChE levels are associated with the postural behavior of the animal.

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Received June 21st, 1955