le dosage est réalisé par spectrophotométrie en cuves de 1 cm, avec un coefficient de correction de 1,25 tenant compte du taux de récupération de la protoporphyrine. Les valeurs normales sont inférieures à 55 γ/100 ml de globules rouges.

Résultats. (Tableau.) Chez 11 malades les chiffres obtenus sont normaux. Dans l'observation n° 13, après 48 h de traitement, les PPE étaient à 72 γ. Dans l'observation n° 2, concernant un jeune homme de 15 ans traité depuis 1 mois à la dose de 1 g par jour, elles étaient de 114 γ. Enfin, chez un homme de 60 ans soigné à la dose de 1,5 g/jour (observation n° 6), les PPE étaient à 298 γ et 239 γ aux 23e et 24e jours de traitement; au 60e jour, elles étaient redevenues normales (41 γ) alors que la griséofulvine était poursuivie.

Commentaires. RIMINGTON[4] en 1963 étudiant les PPE au cours de traitements à la griséofulvine, constate 13 fois sur 51 des chiffres supérieurs à la normale, n'excédant pas 100 γ; cette augmentation persiste après arrêt du traitement 6 fois sur 38 avec un maximum de 90 γ; il n'y a aucune corrélation entre l'élévation des PPE et la durée du traitement et aucun parallélisme entre les PPE et fécales. WATSON[5] dans 14 cas trouve des chiffres normaux. LOCHHEAD[7] observe chez un malade traité depuis 1 an des PPE à 552 γ; chez 6 autres malades les chiffres sont normaux.

L'hyperprotoporphyrie érythrocytaire induite par la griséofulvine semble donc habituellement modérée, ne dépassant pas deux fois les valeurs normales, puisque des chiffres nettement pathologiques n'ont été constatés que dans 1 cas de LOCHHEAD[7] et chez un de nos malades. Cependant, il est probable que cette élévation soit trés transitoire et donc plus fréquente que ne le laisserait penser les résultats; dans note observation n° 6 l'hyperprotoporphyrie globulaire a régressé spontanément. Le mécanisme d'action de la griséofulvine n'est pas encore parfaitement précisé. Pour DE MATTEIS et RIMINGTON[1], chez le rat la griséofulvine augmenterait la production des protoporphyrines à la fois au niveau du foie et de la mœlle. L'action toxique directe sur le foie semble certaine comme le suggèrent les travaux de GRANICK[8] sur l'embryon de poulet, l'apparition de cancer hépatique chez le rat[9], la surcharge hépatique en protoporphyrines aussi bien chez l'animal[1], que chez l'homme[5], les poussées évolutives déclanchées par la griséofulvine dans les porphyries hépatiques avec perturbation des épreuves fonctionnelles hépatiques[3,2]. In vitro chez l'animal, on note une augmentation de l'activité de l'AAL synthétase[3] et de l'AAL déshydrase[7] hépatiques; mais ces perturbations ne sont probablement que secondaires à une atteinte des processus d'oxydoréduction par inhibition de la NADH oxydase (LABBE[10]) qui assure la conversion du NADH en NAD.

Quand à l'action érythropoiétique elle ne serait pas directe mais secondaire à l'atteinte hépatique. Pour NAKAO[11] l'élévation des protoporphyrines érythrocytaires ne serait qu'un phénomène passif secondaire à la surcharge hépatique en porphyrines. La protoporphyrine en excès dans le foie serait pour une part excrétée dans les féces et pour une autre introduite dans la synthèse de l'hème permettant d'expliquer la composante érythropoiétique comme secondaire à l'atteinte hépatique.

N°	Sexe	Age	Dose journalière de griséofulvine (g)	Protop. érythrop. avant traitement (γ)	Protop. érythrop. en cours de traitement (γ)	
1	♀	34	1	non pratiqué	9	15e jour
2	♂	15	1	non pratiqué	114	30e jour
3	♂	40	1	non pratiqué	31	15e jour
4	♂	45	1,5	non pratiqué	30	20e jour
5	♂	35	1,5	non pratiqué	34	13e jour
6	♂	60	1	non pratiqué	298	23e jour
					239	24e jour
					41	54e jour
7	♂	63	1,5	25	24	19e jour
8	♀	65	1	30	32	4e jour
9	♂	68	1,5	48	38	12e jour
10	♂	40	1,5	39	25	15e jour
11	♂	51	1	non pratiqué	43	15e jour
12	♂	45	1	non pratiqué	37	2 mois
13	♂	38	1	non pratiqué	72	2 jours
14	♂	69	1,5	30	26	20e jour

Summary. Erythrocyte protoporphyrin have been measured in 14 patients treated for fungal infections by griseofulvin. In 3 cases there was a rise that reached 298 γ/100 ml red cells. In 1 case this returned to normal values without interruption of treatment. The red-cell protoporphyrin rise is perhaps secondary to griseofulvin hepatic toxicity.

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Service de Dermatologie, Hopital de l'Antiquaille, F-69 Lyon 5e (France), 23 septembre 1969.

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Local Hydrogen-Clearance and Po_2- Measurements in Micro-Areas of the Rat Brain

LÜBBERS et al.[1] measured the oxygen tension of exposed cerebral cortex by means of small platinum microelectrodes and recorded low Po_2-values ranging between 1 and 3 mm Hg in different areas of the cortex despite the fact that the EEG patterns were normal. In order to decide whether these low Po_2-values were a result of a low regional cerebral blood flow or of a high oxygen consumption rate of the brain tissue, a new polarographic method was developed. Employing the same platinum needle, local oxygen partial pressure values and hydrogen clearance curves were recorded at the same point of the brain tissue.

The use of platinum microelectrodes for oxygen measurements is well known from the work of CATER and SILVER[2], SILVER[3,4], CATER[5], FATT[6], KUNZE[7], LÜBBERS[8,9], WHALEN[10], and others. HYMANS[11], AUCKLAND, BOWER and BERLINER[12], FIESCHI, BOZZAO and AGNOLI[13], NEELY, TURNER, HARDY and GODFREY[14], and others used the platinum or platinum-palladium electrodes for hydrogen-clearance measurements. From the time-

response-curve of hydrogen-clearance, regional cerebral blood flow is calculated.

The experimental investigation presented in this paper is based on the hydrogen and the oxygen polarogram. The assumption to be tested is that no reciprocal influence of the 2 gases occurs at the platinum surface. If this could be positively demonstrated, it should be possible to measure oxygen tension and local blood flow with the same platinum needle.

Methods. (a) Construction and calibration of the platinum needle. The well-known method developed by CATER and SILVER[2], and described by SILVER[4], GULD[15] and others was used. The electrodes had tip diameters of 1–10 μ and were membrane covered. Prior to calibration the electrodes were set to a negative polarization voltage of 800 mV in order to obtain constant surface conditions on the silicon membrane. The electrodes were calibrated with a 0.2*M* KCl solution. Between calibration curves measured at the end and the beginning of each experiment, maximum changes of about 5–10% were obtained.

(b) Experimental procedure. Albino rats (about 250 g body wt.) were used and anaesthetized with Nembutal (40 mg/kg body wt.). The head of the rats was fixed in a stereotactic micromanipulator of LPC-company (France). Small holes of 1–2 mm. diameter were drilled into the skull cap of the frontal and occipital part of the rat brain.

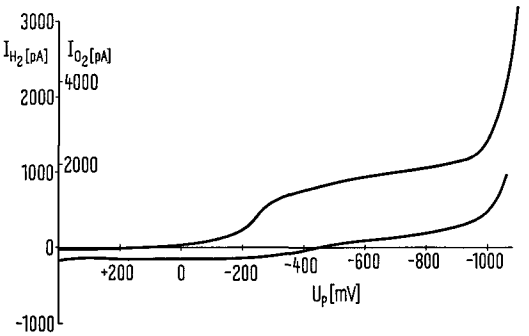

Fig. 1. Oxygen and hydrogen polarogram of a 5 μ platinum microelectrode. Ordinate (left side): Current of hydrogen oxidation process. Ordinate (right side): Current of oxygen reduction process. Abscissa: Polarization voltage (mV).

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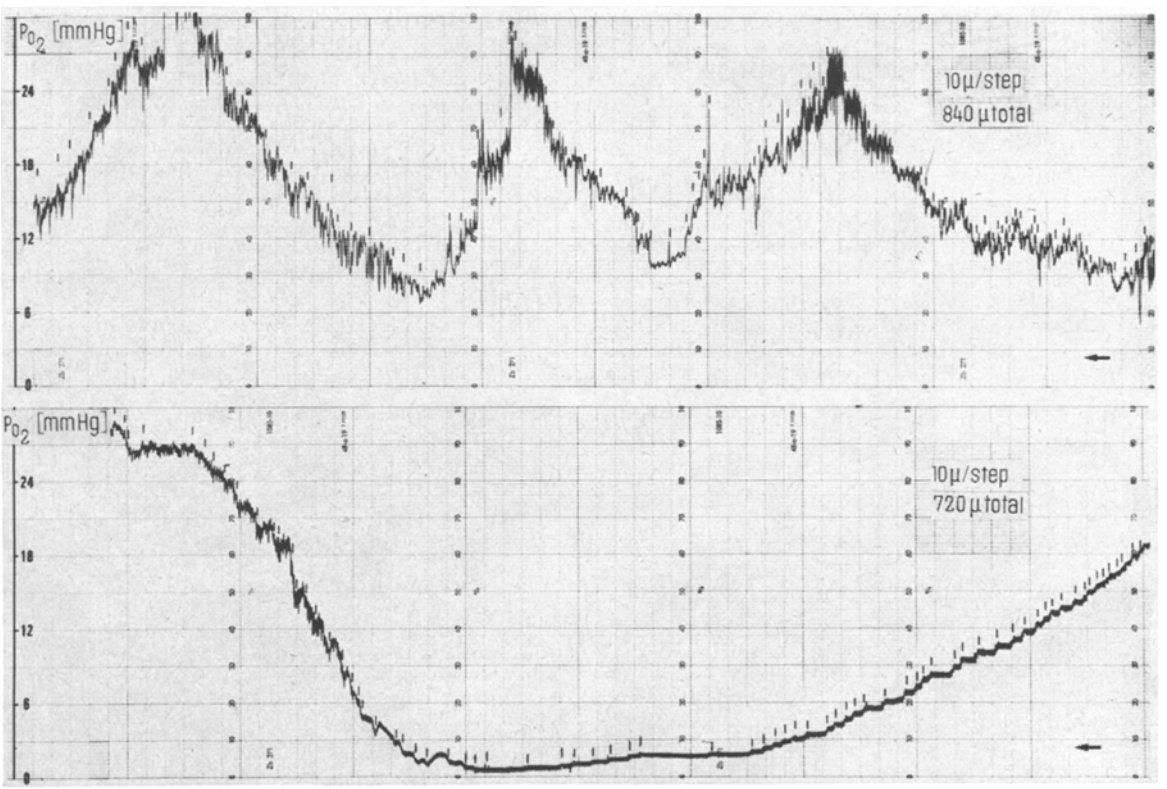

Fig. 2. Upper trace: Po_2 of the rat brain. The thin lines marking the movement of the micromanipulator in steps of 10 μ. Lower trace: Po_2 decrease from the brain surface into the tissue (registration from the right- to the left-hand corner of the Figure).

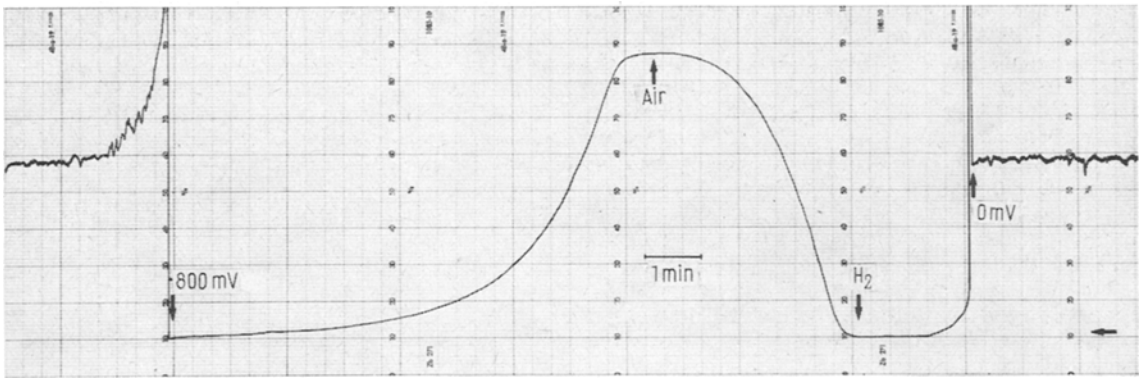

Fig. 3. Combination of Po_2- and H_2-clearance measurement. The change in polarization voltage, as well as in inspiratory gas mixtures, is marked by arrows. At the right- and left-hand corner of the Figure, the Po_2 registration and in the middle of the Figure the hydrogen registration can be seen.

The rats were intubated and breathed spontaneously. The micromanipulator was moved forwards 10 μ per step. At definite parts of the brain tissue, especially at Po_2 maximum and minimum values, polarization voltage was changed from 800 mV negative to 200 mV positive. Then the animals breathed a gas mixture containing hydrogen instead of nitrogen. After saturation of the brain tissue it was switched over to normal air. After that the hydrogen clearance was recorded.

Results and discussion. In this investigation the combined oxygen-hydrogen measurement with a single platinum microelectrode was examined. By means of the O_2- and H_2-polarogram (Figure 1) it can be shown that the current produced by the reduction of O_2 molecules at the platinum surface is zero if a positive polarization voltage of 200 mV is applied. For oxygen measurement a negative polarization voltage of 800 mV was applied. At 800 mV negative the current produced by hydrogen molecules is about 0.1% of that of the O_2 molecules. No interrelationship between oxygen and hydrogen measurements could be seen under these conditions. O_2 profiles as illustrated in the upper trace of Figure 2 could rarely be recorded in our experiments (material from about 25 rats). Typically, the Po_2-differences are smaller. Occasionally, a decrease in the regional oxygen partial pressure within the first 500 μ from the surface of the brain was observed when the platinum needles were moved centrally perpendicular to the brain surface (Figure 2, lower trace). Under these conditions it has to be taken into consideration that the big electrode shafts might diminish regional blood flow, especially that of the venous system which runs mainly on the surface of the brain tissue. Furthermore, FATT[6] observed a decrease of Po_2-recording when mechanical pressure is applied to the tip of the microelectrode. We suppose that the mechanical resistance of the pia caused the decrease of the Po_2-reading. The low Po_2-values agree well with the relatively high half-time values obtained for the fast component of the hydrogen curves.

In Figure 3 a combination of Po_2- and hydrogen-clearance measurements is illustrated. After a change in polarization voltage only a short time is necessary to obtain a constant H_2-value. After saturation of the brain tissue with hydrogen, the inspired gas was changed to air and hydrogen-clearance curve was recorded. The half-time necessary to reach half of the initial values of the hydrogen concentration amounted to about 2.15–4.45 min, the corresponding Po_2-values measures in about twenty Po_2–H_2-clearance combinations were 1–35 mm Hg, in a few cases the oxygen-tension values were greater.

In about 20 combined Po_2- and H_2-clearance measurements, the reproducibility of this kind of experiment was demonstrated (Figure 3). However, only 10% of the platinum needles which were suitable for oxygen measurement could be used for both oxygen and hydrogen measurements. A correlation between Po_2 and local blood flow values could not yet be proved by our results.

Résumé. La pression partielle de l'oxygène et la «clearance» de l'hydrogène ont été mesurées dans des régions circonscrites. Les deux valeurs sont enregistrées par la même microélectrode de platine (diamètre de la pointe 10 μ). Cette méthode nouvelle est appliquée dans des expériences faites sur le cerveau de Rats narcotisés et on est capable d'évaluer les inhomogénités locales de l'apport d'oxygène dépendant du flux du sang.

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The Responsiveness of Acoustic Area after Stimulation of the Caudate Nucleus

Recent electrophysiological data seem to indicate that peripheral stimulation of various origin may activate the caudate nucleus[1–4]. The hypothesis has been suggested that the caudate nucleus participates in the control of specific and non-specific sensory afferents[5–7]. The present experiments were prompted by the relationship between caudate nucleus and EEG activity[8–11] to demonstrate the control of the sensory input in the neocortex by the caudate nucleus.

Material and method. The experiments have been carried out on 36 cats, curarized, with local anaesthesia of painful points or anaesthetized with pentobarbital or with chronically implanted electrodes. We recorded the evoked potentials in the acoustic area with or without conditioning stimulation of the caudate nucleus, periodically varying the intensity of the click sound energy (expressed in dB below the arbitrary reference level). We used conventional stereotaxis and electrophysiological