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KNJIGA XVII

ODJELJENJE MEDICINSKIH NAUKA
KNJIGA 4.

MEĐUNARODNI SIMPOZIJUM

O EKSPERIMENTALNOM TREMORU

1 — 3. APRIL 1971. GODINE

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SZ. TÓTH, É. OROSZ AND J. JUHASZ

THE EFFECT OF SOME PARKINSONOGEN DRUGS ON THE CEREBRAL ELECTRICAL ACTIVITY OF THE CAT.

A great number of drugs are known which in animal experiments and in clinical use, as by effect, produce hypokinetic rigid syndrom. Without looking at the experimental side of the question, the problem is very important because it emphasizes, that Parkinson syndrom is a rather general type of reaction of the nervous system or moreover the motorium, which can be elecited by different actions. This contradict the presumption of Poskanzer and Schwab (1963), that Parkinsonism is in the process of disappearing, because epidemical encephalitis epidemia did not occured since World War I. We must range the Parkinson syndrom — not in it's mechanism, but in it's nature — as epilepsy or as hyperkinetic syndrom, which occurs with a certain type of injury of the nervous system, quite independently from the reason that causes the injury or the functional disturbance.

It is well known that the electrical signs of the Parkinson disease are very scarce, not specific or can not be observed at all, (Hughes, 1966) mainly when not taking into consideration attempts of activation tests. (Tóth — Tomka, 1968). Therefore, it is the more interesting that parkinsonogen neurolept drugs change the cerebral electrical activity, and so enable the investigation of the effect producing Parkinson syndrom, by a routine clinical method. These considerations induce us to carry out model investigations of some neurolept drugs in animal experiments.

21 curarized and respirated cats were used for the experiment. 3 pairs of electrodes were placed into the skull on both sides. The deep electrodes were introduced by stereotactic way into the thalamus (n. V—L), pallidum and the mesencephalic reticular system on both sides.

The cerebral activity and evoked potencials gained by sound and light stimuli were registered by a 16-channel ELEMA EEG apparatus. The femoral arterial pressure was also continously registered. Drugs were administered intravenously. 2,5 mg of Dehydrobenzperidol (DHBP), 1 mg of Rausedyl (Reserpine) and 1,25 mg of Haloperidol were administered repeatedly. (The largest doses of DHBP contained 4 x 7,5 mg, of Rausedyl 5 x 1 mg, and of Haloperidol 4 x 1,25 mg.).

We investigated the action of the combination of the three drugs mentioned and also the combination with pentamethylentetrazol.

According to our experiences the three drugs change the cerebral electrical activity in the same way but to different degrees. With all the tree drugs, just after the injection, first the activity is desynchronized and the beta activity dominates. This activity qickly disappeares and gives way to an extensive alfa-theta activity. Frequently the alfa, theta waves occur in short bursts with high amplitudes. (Fig. 1. a), b), c). (Within these bursts many sharp, spikelike waves occure diffusely. (Fig. 2. a), b). (The bursts consists — mainly after Haloperidol — of sinusoid

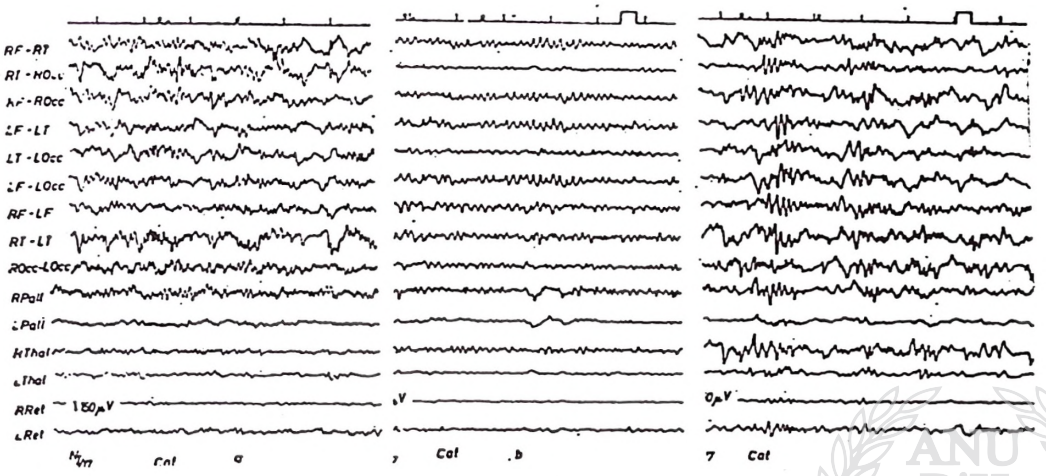

Fig. 1

Cat N I/17

a) Activity without medication
b) After 7,5 mg DHBP: slowing down and stable alfa activity
c) After 2 x 7,5 mg DHBP: alfa activity in short groups

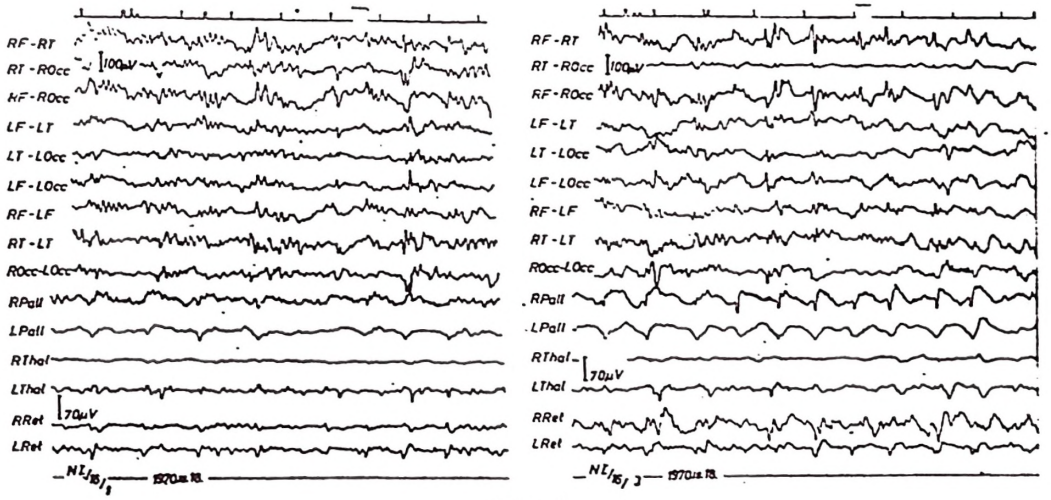

Fig. 2

Cat N I/16

a) Unmedicated state
b) After 7,5 mg DHBP: sharp, spikelike waves appeare

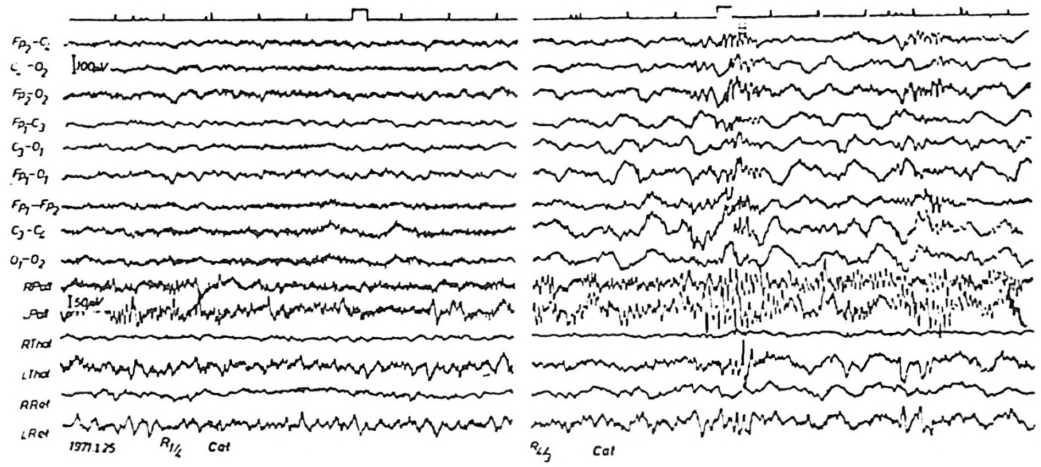

Fig. 3

Cat R/4.
a) Unmedicated state.
b) After 1,25 mg Haloperidol: general slowing down and sinusoid alfa-theta groups appeare. Increasing activity of the deep electrodes.

theta-delta waves combined with sharp waves. (Fig. 3. a), b). With higher doses the electrical picture does not change essentially, but more and more slow waves appeare diffusely in the activity. When no more drugs are given, the changed activity prevails for hours. Under the effect of rising doses the activity of the thalamus, pallidum and reticular substance is more and more expressed. This is particularly remarkable in the thalamic activity because without drugs this activity is the

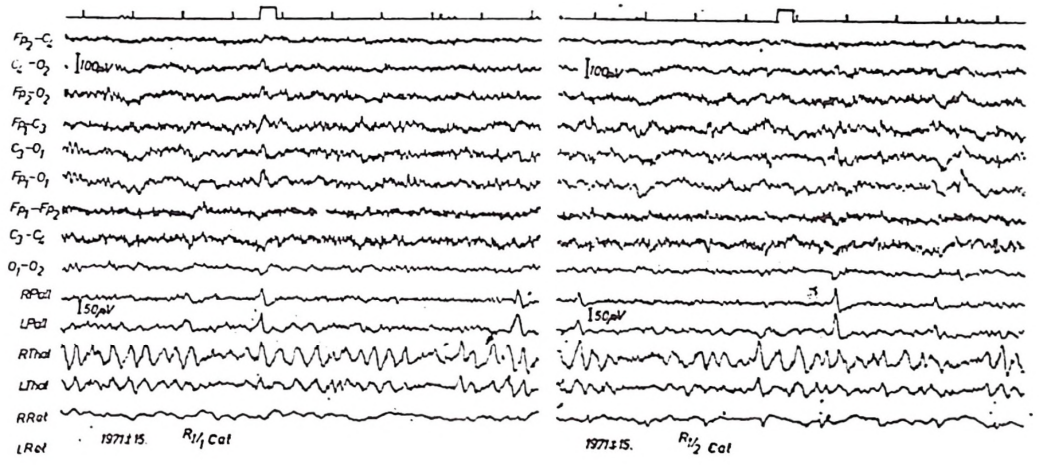

Fig. 4

Cat R/1.
a) Unmedicated state. During stimulation by light no evoked potencials.
b) By sound stimulation evoked potencials can be seen on the reticular electrodes and sporadically on the cortical ones too.

poorest. Giving Rausedyl (Reserpine) Haloperidol and DHBP in combination or one after the other their effect on the cerebral electrical activity is more marked than when given only one of them repeatedly. (Fig. 4. a), b), and Fig. 5. a), b).

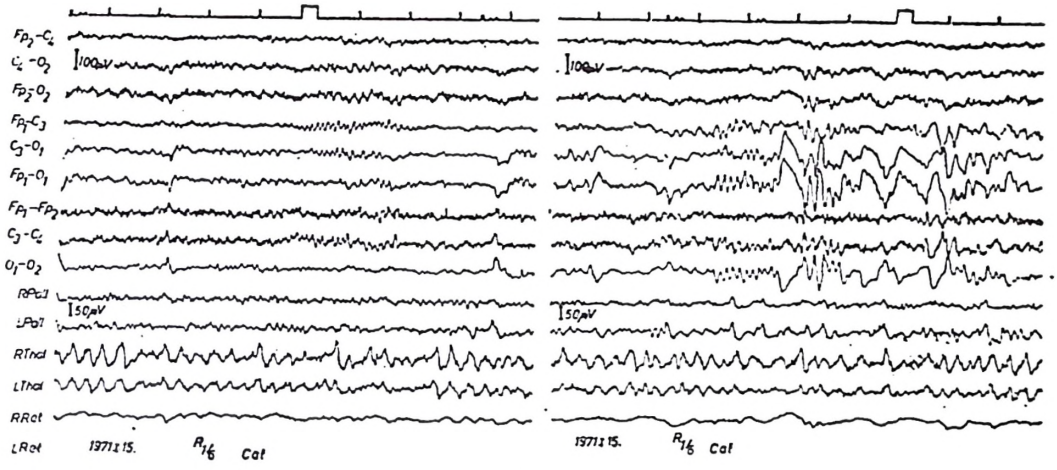

Fig. 5

Cat R/1.

a) *After 2 x 0,5 mg Rausedyl (Reserpine): sinusoid alfa activity*

b) *After 2 x 0,5 mg Rausedyl + 6,25 mg DHBP: sinusoid groups of alfa-theta waves can be seen with high amplitudes.*

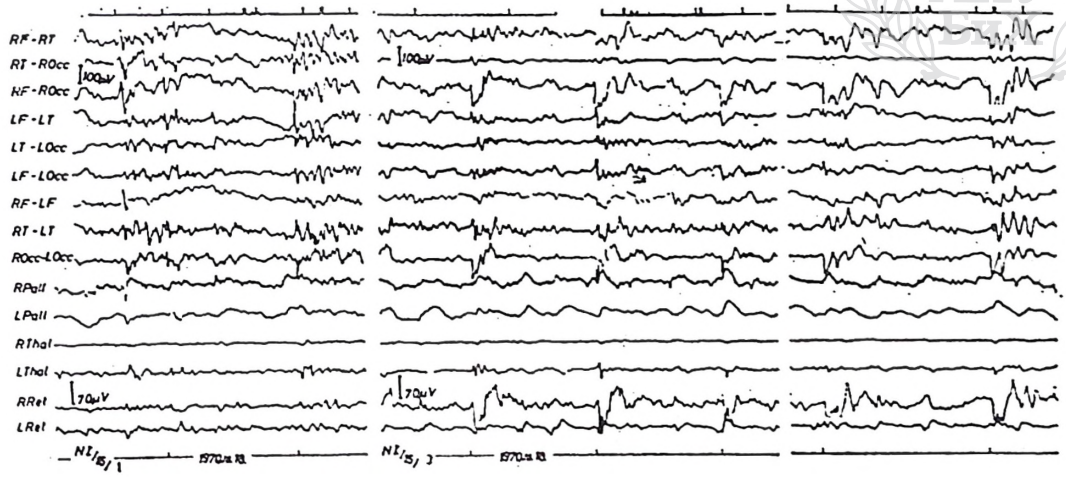

Fig. 6

Cat N 1/16

a) *Unmedicated state. Definite responses can not be seen on light stimuli.*

b) *After 7,5 mg DHBP: definite responses, in accordance with the stimuli, evoked by light.*

c) *After 7,5 mg DHBP: marked multiple discharges evoked by sound stimuli. (In unmedicated state response was not to be gained by sound).*

After neurolept premedication, the irritative signs evoked by pentamethylen-tetrazol are more intensive and more prevalent. This effect is most marked after DHBP, less expressed after Haloperidol and least notable after Rausedyl. After DHBP the effect may reach such intensity that repeated electrical seizures appeare, for a prolonged time.

Evoked potencials of sound and light stimuli are also changed by the effect of DHBP, Rausedyl and Haloperidol. After the administration of the three drugs the amplitudes of the evoked potencials and the number of after-discharges increase. The evoked response is becoming stable, or more exactly, the responses follow the stimuli more systematically than without medication. (Fig. 4. a), b), Fig. 6. a), b), c), Fig. 7. a), b), Fig. 8. a), b.)

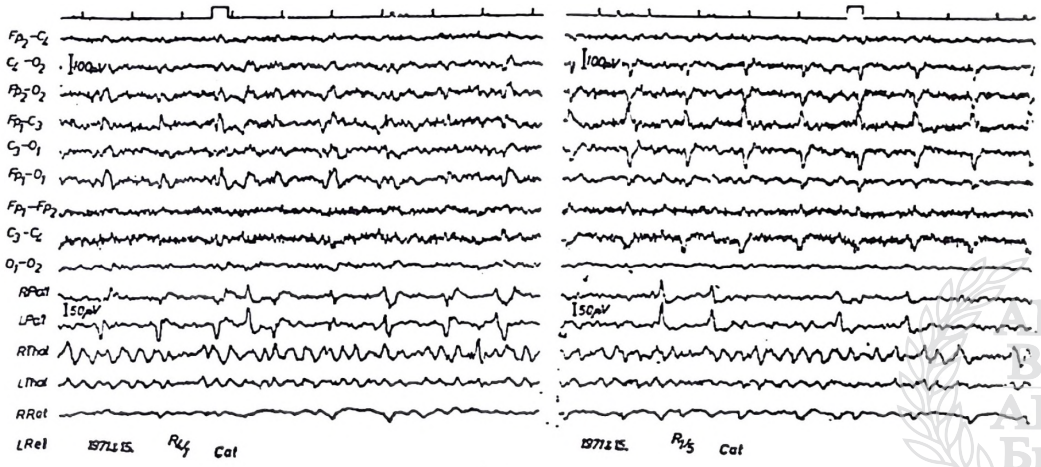

Fig. 7

Cat R/1.

a) After 0,5 mg Rausedyl (Reserpine), stimulation by light: pronounced evoked potencials on the pallidar and cortical electrodes.

b) After 0,5 mg Rausedyl, sound stimulation: evoked potencials on the reticular and cortical electrodes.

(The unmedicated and stimulated state see in Fig. 4 a) and b).)

In literature many references can be found in connection with the cerebral electrical changes observed also by us. According to Raoul Jeri (1956) Reserpine activates the petit mal and grand mal activity. Rinaldi and Himwitch (1953), observed the activation of the reticular substance due to Reserpine. Sigg and Schneider's (1957) examinations are similar to those mentioned above. According to their observations Reserpine activates convulsive activity in the rhinencephalon. Gonnard and Co. (1956) mention the convulsant supporting effect of Reserpine. Many authors are rather interested to find relation between the tranquillant effect and the EEG signs of the said drugs. (Liberson, 1956, Monnier and Gangloff 1956, Ekiert and coll. 1959, Wilson and coll. 1964).

Some authors attribute to Reserpine and Haloperidol once an inhibitory, at other times excitatory effect, depending on the basic function of the brain. (Kamenskaja and coll, 1965, Geyer and coll. 1967). No

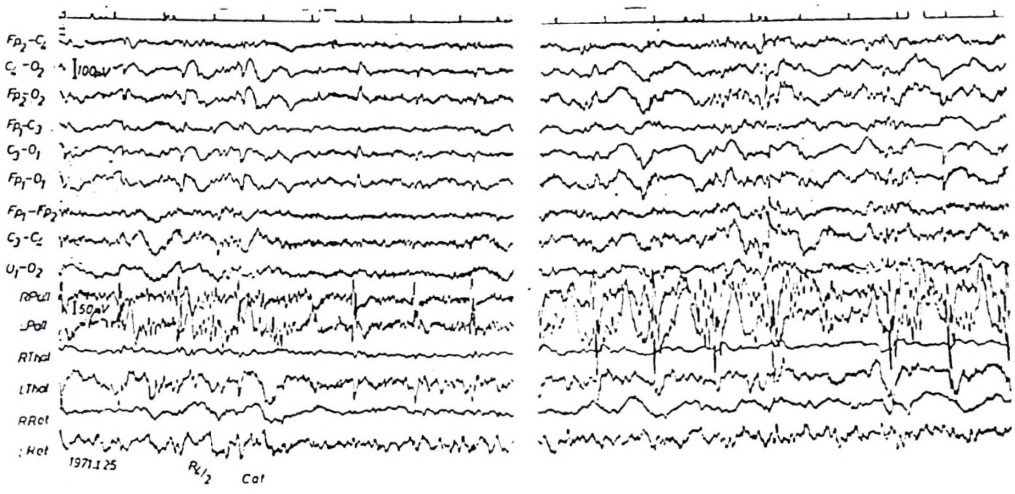

Fig. 8

a) Unmedicated state. Evoked potencials by light stimuli on the pallidar and thalamic electrodes, sporadically on the cortical ones too.

b) After 2 x 1,25 mg Haloperidol: The evoked potencials are more marked both on the cortical and the deep electrodes.

data relating to the effect of DHBP on the cerebral electrical activity can be found, but our investigations carried out in neuroleptanalgesia (Orosz and coll, Tóth and coll.) reinforce our results described above. We did not find any literary contributions which deal with the parkinsonogenic effect of neurolept drugs in connection with EEG signs either.

The interpretation of this interrelation is by no means easy and can only be approached with due care.

No doubt however, that EEG and deep electrode examinations of patients with Parkinson syndrom may indicate hypofunction, — or perhaps the relative hyperfunction of certain areas — and the decrease of reactibility.

In contrast to the above, the change of the electrical activity of the brain, due to neurolept drugs is indicative of hyperfunction, irritative activity and increased reactibility, in general.

That seems to suggest that the functional disorder leading to dyskinesia takes place on a different level in Parkinsonism than in conditions elicited by the effect of neurolept drugs.

It is worth mentioning that the stable and extensive alfa activity is observable both in Parkinsonism and in condition due to neurolept drugs.

Evoked responses gained under the effect of Rausedyl (Reserpine), Haloperidol and DHBP occur regularly uniformly and with higher amplitudes. This should allow for the conclusion that in this condition selective control function decrease.

SZ. TÓTH, É. OROSZ I J. JUHASZ

EFEKT PARKINSONSKIH LIJEKOVA NA ELEKTRIČNU AKTIVNOST MOZGA

KRATAK SADRŽAJ

U prethodnim ispitivanjima pokušali smo da pronađemo metode koje bi nam mogle pružiti priliku da procijenimo operativni kapacitet pacijenata sa Parkinsonovom bolešću. Ispitivanja smo bazirali na pretpostavci da se reaktivnost mozga mora izmijeniti tokom bolesti i da mogu da postoje korelacije između reakcije na odgovarajuće opterećenje i reakcije na hirurške zahvate.

U sadašnjim ispitivanjima analizirali smo u vezi sa naprijed navedenim model-uslove i razvijenu reaktibilnost mozga koju su izazvali parkinsonski lijekovi.

U toku eksperimenata mačkama smo dali povećane količine dehydro-benz-perydola, rauwolfia derivata i Haloperidol. Proučavali smo promjene električne aktivnosti mozga i izazvane reakcije na svjetlosne i zvučne stimulanse. Primijetili smo da je EEG pacijenata sa Parkinsonovom bolešću sličan EEG-u koji su prouzrokovali parkinsonski lijekovi. Reakcija na svjetlosne i zvučne stimulanse mijenja se pod uticajem parkinsonskih lijekova (isto tako i reakcije na električne stimulanse, kako smo vidjeli kod stereotaktičnih hirurških zahvata). Intenzitet izazvanih reakcija raste sa povećanjem količine lijekova, što nam može pokazati hiperaktivnost stimuliranog sistema, ali i njegovu nestabilnost. U stupnju izazvanih reakcija na korteks i supkortikalne ganglije (talamus, n. ventrolateralis, pallidum, substantia reticularis) postoji promjena uglavnom u pravcu supkortikalnih ganglija.

Na osnovu naših rezultata pokušali smo da analiziramo mehanizam djelovanja parkinsonskih lijekova. Uporedili smo efekt Parkinsonovog sindroma na ljudskom kliničkom materijalu sa eksperimentalnim parkinsonskim efektom.

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