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KNJIGA XVII

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MEĐUNARODNI SIMPOZIJUM

O EKSPERIMENTALNOM TREMORU

1 — 3. APRIL 1971. GODINE

Urednik
PAVEL ŠTERN,
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K. KENDEL AND U. BECK

NOCTURNAL SLEEP IN PATIENTS SUFFERING FROM PARKINSON'S DISEASE UNDER L-DOPA TREATMENT

Experiments on animals with monoaminoacids lead to the conclusion that L-DOPA acts on the sleeping mechanisms, especially the sleep-cycle. J o u v e t (1) postulated the existence of neurones with a special sensitivity for monoaminoacids which are responsible for the fundamentally different sleep phases, i. e. the synchronized and desynchronized phases. W y a t t et al. (2) found distinctively decreased REM-phases of sleep but unchanged or slightly increased synchronized sleep in patients treated with-Para-Chlorophenylalanine and L-DOPA. Beside the therapeutic effect on the Parkinson symptoms, an influence on the sleep cycle in these patients is probable under treatment with high dosage of L-DOPA.

15 polygraphical night-sleep EEG registrations were performed in 9 patients suffering from Parkinson's disease before and 12 registrations during L-DOPA therapy of various dosage. We used 4 EEG-registrations by adhesive electrodes and recorded the right and left occipital and the right and left precentral against a vertex electrode. Eye movements, the EMG of musculus mentalis, ECG and respiration were registered too. On the automatic TÖNNIES-EEG-interval-spectrum-analysator, (3) one occipital recording, the eye movements and the EMG were additionally registered. With this method the time-interval between 2 zero points of EEG waves is electronically measured. The trigger-impulse for this time-measuring is corrected in dependence of the amplitude and the reversal points of the single EEG-waves and is not influenced by base-line drives of the EEG. Each of the measured intervals is transformed into the corresponding frequency and is burned into the registration paper as a little black point. Thus the ordinate of the registrating paper shows the frequencies of the measured EEG-waves from 1 to 30 Hz. The speed of the paper stripe amounts to 2,5 mm/min. A night--sleep registration of 8 hours is therefore visible on paper stripe which is 120 cm long. Because of this extremely slow paper speed the muscle action potentials which are registered as stripes appear as a black ribbon. The broadth of the black ribbon allows an orientation about the momentary muscle tone. Rapid eye movements are now additionally registered on a third channel as stripes and help diagnosing the REM--phases.

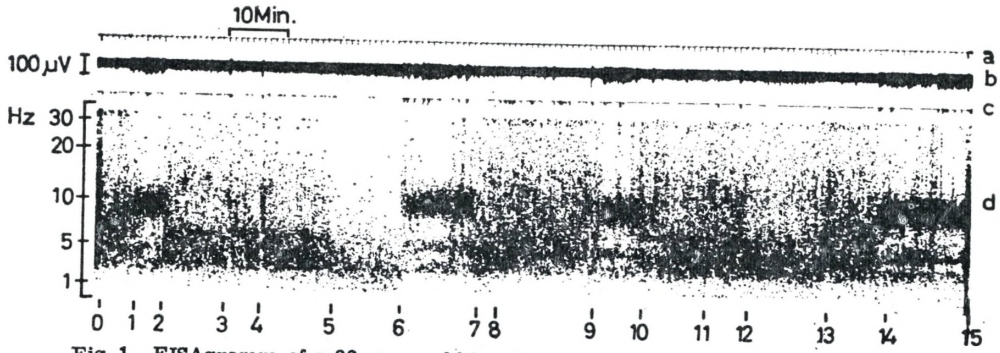

Fig. 1 EISAgramm of a 22 years old healthy student
a Time (sec)
b EEG - amplitude
c Eye movements
d EEG frequency spectrum
numbers 0 - 15 = different sleep stages
(2 = falling asleep, 8 - 9 REM, 14 = awaking)

When evaluating the night-sleep registrations by means of the EISA-gram each sleep stage can be recognized. In case of uncertainties it can be examined by comparison with the usual EEG-registration. The definition of sleep stages is based upon the international statements by Rechtschaffen and Kales, (4) taking stage I and II as light sleep and stage III and IV as deep sleep.

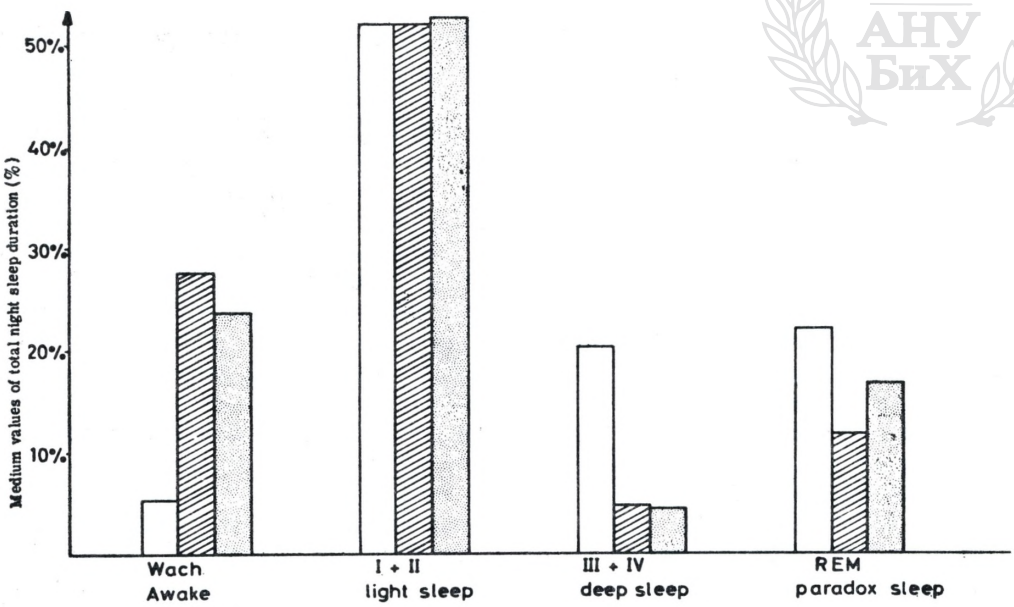

Fig. 2 Sleep stages in patients with Parkinsonism before and during L-DOPA treatment
(Percentual medium values of total sleep duration of the different groups)
Normal group
Patients with Parkinsonism without L-DOPA treatment
Patients with Parkinsonism during L-DOPA treatment
Ke/71

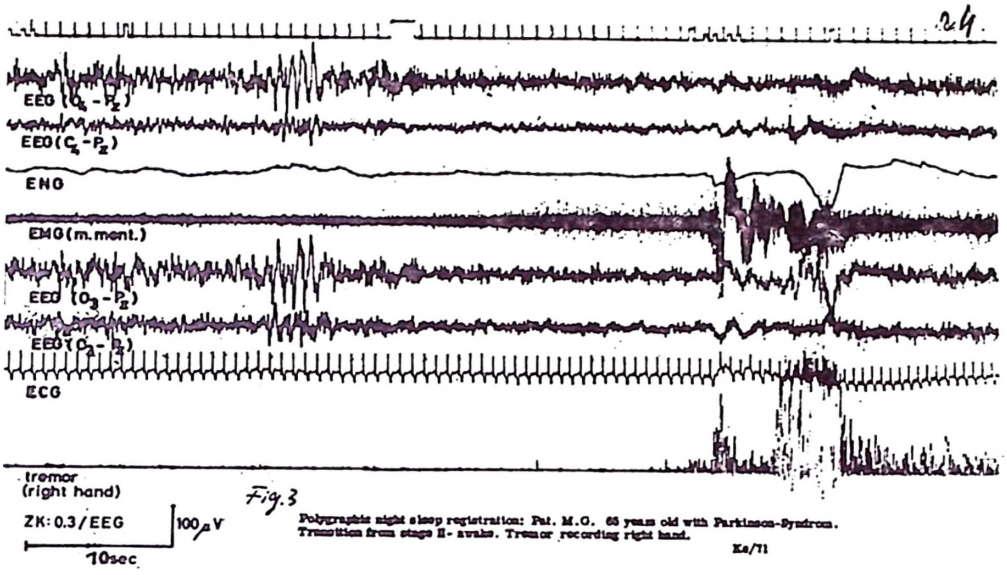

Fig. 3 Polygraphic night sleep registration: Pat. M.G. 65 years old with Parkinson-Syndrom. Transition from stage II - awake. Tremor recording right hand.

Beside the quantitative analysis of the sleep stages, the ECG, respiration excursions and tremor were taken into consideration. The influence of L-DOPA on tremor in the different stages of sleep will be especially investigated and compared with the tremor intensity during daytime.

We found that the night sleep of patients suffering from Parkinson's disease without therapy is characterized by abnormalities concerning the duration and distribution of the single stages. Hitherto our investigations show a tendency to normalization of the disturbed night sleep under treatment with L-DOPA. The total duration of sleep and the percentage of REM sleep rise. The sequence of the single sleep stages in Parkinson's disease is disturbed: an investigation of night sleep of healthy young adults shows that the stage REM follows stages I and II (B and C) in 98%, while in Parkinson patients without L-DOPA this percentage is 63% and after L-DOPA treatment 83%. The »REM-Latency« i. e. the duration from the onset of sleep to the first REM stage rises significantly under treatment with L-DOPA.

The comparison of the percentual share of single sleep stages and night waking phases in Parkinson patients under and without L-DOPA treatment shows no difference concerning light sleep. The share of waking phases in patients with Parkinson's disease is considerably higher as in a comparable group of healthy persons. During L-DOPA therapy the portion of the night waking phases decreases a little. In comparison with the normal group it must, however, be mentioned that this group of healthy persons consists of younger subjects. This age-difference is propably responsible for the considerably smaller share of deep sleep in patients with out and during L-DOPA treatment. Though theoretically unexpected, an increase of REM-sleep can be seen in our series during a REM-rebound as described by W y a t t (2) et al. in the second half L-DOPA treatment. A possible explanation of this observation might be of the night after preceding supression of REM-sleep. This problem needs further investigation.

Only two patients of our series showed an evident extrapyramidal rest tremor. This number is comparatively small as patients with akinesia were preferred for L-DOPA treatment. — The tremor was recorded with a mechanical-electronical-transducer (Accelerometer Burchardt). The transducer was applicated on the hand showing the strongest tremor--intensity.

Both patients with pronounced 4—5 and 5—6/sec rest. tremor in day time showed tremor during night sleep registration only in connection with body movements and appearance of EEG basic rhythm for a few seconds. The tremor frequency was the same as that of the rest tremor in day-time. There was no tremor during synchronized sleep in both subjects. One patient showed tremor with a frequency of 4,5/sec during REM-sleep as in the waking state. The tremor lasted once longer than 20 sec. in a REM-phase.

Summarizing can be stated that night sleep in patients with Parkinson's disease shows deviations from normal sleep. During L-DOPA treatment a tendency to normalization is evident. In patients with tremor a disappearance of tremor in synchronized sleep can be expected. Almost regularly a reappearance of tremor during body movements can be observed. During REM-sleep an activation of tremor may occur.

K. KENDEL I U. BECK

NOĆNI SAN PACIJENATA BOLESNIH OD PARKINSONOVE BOLESTI POD TRETMANOM L-DOPOM

KRATAK SADRŽAJ

Eksperimenti vršeni monoaminokiselinama na životinjama doveli su do zaključka da L-dopa djeluje na mehanizme sna, naročito na ciklusne. Jouvet i saradnici pretpostavili su postojanje neurona sa specijalnim senzitivitetom za monoaminokiseline koji su odgovorni za fundamentalno različite faze sna, tj. sinhronizirane i desinhronizirane faze. Wyatt i saradnici su našli znatan porast REM-faza sna, ali nepromijenjen ili vrlo mali porast sinhroniziranog sna kod pacijenata liječenih para-hlorofenilalalinom i L-DOPOM. Pored terapeutskog efekta na parkinsonske simptome, vjerovatno uslijed tretmana visokim dozama L-dopa, pojavilo se djelovanje na ciklus sna tih pacijenata.

Izvršen je poligrafski EEG noćnog sna pacijenata sa Parkinsonovom bolesti prije i za vrijeme tretmana različitim doziranjem L-DOPOM. Svi EEG noćnog sna bili su simultano registrirani preko EEG Interval Spectrum Analysatora (EISA, Tonnies). Serije još nisu završene.

Našli smo da je noćni san pacijenata bolesnih od Parkinsonove bolesti bez terapije okarakterisan nepravilnostima u trajanju i raspodjeli *jednostavnih stupnjeva*. Dosada su naša ispitivanja pokazala tendenciju ka normaliziranju nemirnog noćnog sna pod tretmanom L-DOPA; ukupno trajanje sna i postotak REM-sna su povećani. Niz jednostavnih

stupnjeva sna kod Parkinsonskog sindroma je poremećen: ispitivanje noćnog sna zdravih mlađih punoljetnih ljudi pokazuje da stupanj »REM« slijedi stupnjeve I i II (B i C) u 98% slučajeva, dok kod bolesnika sa Parkinsonskom bolešću bez tretmana L-DOPOM taj postotak iznosi 63%, a nakon tretmana L-DOPOM 83%. REM-latentnost« (trajanje od početka sna do prvog REM-stupnja) povećava se znatno prilikom tretmana L-DOPOM.

Pored kvantitativnih analiza stupnjeva sna, registrirani su EKG, pokreti disanja i motorna aktivnost (tremor). Djelovanje L-DOPE na tremor u raznim stupnjevima sna specijalno je istraživano i upoređeno s intenzitetom u toku dana.

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DISCUSSION

Dimitrijević: Could you elaborate a little on mechanism which are influenced by L-DOPA? Are they pharmacological or physiological? I mean often L-DOPA their improves and they become more sleepy because uf their physical activity?

Kendel: To 2) The pharmacological or neurophysiological mechanisms on human sleep under high dosage of L-DOPA are unknown. It may be-and some experiments support this -that a specific influence on the sleep regulation mechanisms exist. But also we had to take in consideration unspecific components for instanc an improvement of akinesia and therefore a better sleep.