MULTIPLE LINEAR REGRESSION ANALYSIS OF GRAND MAL AND PETIT MAL FORMS OF EXPERIMENTAL EPILEPSY

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SUMMARY

Relationships between amplitude of penicillin-induced generalized epileptiform signals in different zones of the brain cortex (occipito-frontal bilateral leads, as well as occipital and frontal bipolar leads) were investigated in Wistar rats using multiple linear regression method of analysis. Results were expressed in the form of policycle multigrafs (multidimensional presentation) with the identification of significant ($p<0,1$) negative or positive influences of certain direction between sources of signals. The prevalence of the involvement of left hemispheral cortex into creation of positive type of forward, and back-directed influences was identified, while greater ability to be involved in the creation of negative type of relationships was established for the occipital zone of cortex during 6-h course of generalized seizure activity development. Final stage of the epileptic activity development was characterized by positive relationship's domination. Typical absence spike-wave activity in WAG/rij rats was characterized by the prevalence of positive relationships, which were present between almost all inspected zones of cortex. Besides, minimization of mutually negative relationships when compared with generalized penicillin-induced epilepsy, was also characteristic for WAG/rij ECoG activity. These facts might be in favor of the most pronounced synchronized processes in comparison with epileptic discharges induced by excessive dosage of penicillin solution. Authors came to conclusion that policycle presentation of relationships between amplitude signals, which are generated in different cortical zones, with an emphasis on polifunctional dependence of each investigated index might be of interest for the characteristics of experimental epilpetic process.

KEY WORDS: multiple linear regression, policycle multigraf, generalized penicillin epilepsy, absence epilepsy, spike-wave complexes.

Multiple linear regression might be regarded as the most proper approach for the analysis of systemic relations between number of factors [1, 6]. In accordance to this method, zones (sources) of EEG signals represent by themselves a number of interactive units, all elements of this entity are assumed to be a function of the rest elements of multiplicity of elements.

Hence, it means that relations between different characteristics of bioelectricity, which are simultaneously registered in different zones of cortex, might be of worth for the clarifying dynamic peculiarities of cortical neuronal populations involved into epileptic activity development, and identification of them as elements of proper dynamic systems as well. With the aim of performing of such an analysis the investigation relationships between amplitude of ECoG signals registered in different cortical zones was choosed as a most informative one. That was done because of changes of amplitude are the earliest ones in the course of epileptic activity development.

Determination of the intensity as well as direction of influences between the number of hyperexcited neuronal populations is possible to perform in the course of usage of multiple linear regression method. Hence, clear differences in comparison with the most widely used cross-, auto-correlation methods of EEG interpretation might be defined. Namely, correlation coefficients are remarkable for the presence of some sort of relationships between two points (sources of information), and the final results are contributive to 2D image of brain functions. Meanwhile multiple linear regression method, which was enriched with the theory of errors, possesses an ability to investigate multidimensional relationships between number of indices on the strict basis of quantitative evaluation of the power of influences and identification of the direction of such an influence [5]. Hence, in accordance to the general theory of multiple linear regression, positive influence and negative one were identified [1, 6].

It might be suggested that in the course of penicillin-induced generalized epileptic activity different relations are timely created between different zones of brain cortex. They might be presented in the form of "oriented" (positive or negative) influences of one structure (lead) upon other/s and vice versa. Such characteristic is of interest, because brain cortex is heterogenous with regard to the local seizure threshold, role played in the development of absence and generalized seizure forms of experimental epileptiform activity: oro-facial motor cortex is in charge for the initiating typical spike-wave discharges, while entorhynal cortex initiate generalized seizure form of epileptogenesis [3, 7].

As far as absence and generalized seizures are characterized by different, almost opposite, mechanisms of epileptogenesis [4], the aim of this paper was to investigate relationships between amplitude of seizure potentials in

different cortex zones (left and right hemispheres) after i.p. administration of relatively large dosage of benzilpenicillin solution to Wistar rats and to perform comparative investigations on WAG/rij rats, which are demonstrate typical form of inherited petit mal or absence form of epilepsy [2, 9].

MATHERIALS AND METHODS

Animals

Seven male Wistar rats, and 3 WAG/rij rats of both sex weighting 200-270 g were used as experimental subjects. They were kept under standard laboratory conditions, i.e. constant temperature of 23°C, 60% relative humidity, 12 h dark/light cycles, standard diet and tap water was present *ad libitum.*

Procedures involving animals and their care were conducted according to University guidelines that comply with international laws and policies [European Community Council Directive 86/609, OJ L 358, I, December 12, 1987; Na- tional Institute of Health *Guide for Care and Use of Laboratory Animals*, US National Research Council, 1996].

b) General surgery

Registration electrodes were implanted under Nembutal anesthesia ("Ceva", France, 40 mg/kg, i.p.): two in frontal and two in occipital regions in both hemispheres [8]. Electrodes were fixed to the skull with dental cement. Starting one week after surgery, the rats were handled daily and adapted to the experimental setup.

c) Registration of EEG and model of epileptogenesis

All observations started not earlier than 7 days after operation, and generalized form of epilepsy was induced via i.p. benzilpenicillin sodium salt administration (300.000 IU/100 g, i.p. in a volume of 0,5 ml of saline) to Wistar rats.

Relationships between epileptic activity/discharges in brain cortical zones were investigated, that is why we did not perform registration and analysis of basal EEG. Registration was performed bipolarly:

Lead#1- frontal-occipital zones of left hemisphere (YA1k, ax1);

Lead#2- frontal-occipital zones of right hemisphere (YA2k, ax2);

Lead#3- frontal zones of both hemispheres (YA3k, ax3);

Lead#4- occipital zones of both hemispheres. (YA1k, ax4).

These types of registration permitted us to localize sources of epileptogenesis and, besides, the role of hemispheres (symmetry of EEG activity in the brain) could be inspected.

The analogue data were digitized with a sample frequency of 256 Hz, (resolution of AD converter). Unit of measurement was the mean amplitude of the EEG in a 2 minute period (episode length). Amplitudes were registered using half-period analysis. 30 points (per one hour) which were averaged from all animals were then analyzed and resultant direction and sign of influence between leads (cortical zones) was determined. Time constant used was 0,1 and upper boder of filter-70 Hz.

d) Mathematical approach

The formation of a mathematical model was performed via the usage of multiple linear regression and correlation.

With the aim of creation of mathematical models each of the amplitude index, which was under investigation was regarded as a Y-plotted characteristic marked later on in equations (1.1.-1.24.) with YA1k, YA2k, YA3k and YA4k-figures were in good correspondence to above mentioned number order of bipolar leads. Y-data were calculated on the basis of other variables-amplitudes in other three leads (X-plotted ones, marked as ax1, bx2, cx3 and dx4). The resultant data permit to identify direction and type of proper influence, and to depict it with corresponded arrow on multigraf.

As a result of such a process equations pertinent to multiple liner regression and which were used regularly (on the basis of false-rotation) in our analysis got a typical form:

YA1k=Bo+bx2+cx3+dx4;

YA2k=Bo+ax1+cx3+dx4;

YA3k=Bo+ax1+bx2+dx4;

YA4k=Bo+ax1+bx2+cx3;

Bo-constant factor. Coefficients "a", "b", "c", “d” reflect the level of the influence upon the index which is under analysis of the rest of the members of equation (x1; x2; x3; x4).

The adequate significance of coefficients of regression was regarded via the usage of sigmal deviations of coefficients of regression and the efficacy of regression as a whole was estimated via the calculation of the square coefficient of multiple correlation. The level of statistical significance was accepted at 0,05 (when one-way directed influence was determined) and 0,1 (when two-ways - directed influences were determined).

Geometrical presentation of the equations of the multiple linear regression was performed via usage of policycle multigraphs which contains directed (oriented) influences (positive and negative ones) marked with arrows when they were defined as significant ones. Those relations, which were connected with the increasing of Y function, in case of constant value of X were identified as a positive one. Besides, the error calculation was connected with the evaluating of the "power" of

corresponded relations. And those significant at P<0,1 were marked with solid (significant positive influence) and interrupted (significant negative influence) lines/arrows were marked at final picture.

RESULTS AND DISCUSSION

#I Generalized penicillin-induced epilepsy in Wistar rats.

1.1. Time-course of the penicillin-induced epileptogenesis.

For the characterization of the evolution of benzilpenicillin-induced epileptogenesis 4 registrations were used and for the initial stages (2 hours) of epileptic activity formation 3 additional rats were included as well, which were treated with pharmacons later on.

First seizure potential was evident in 160-577 s after the moment of administration of penicillin solution. The first sign of seizure appeared in 5 out of 7 rats in the left hemisphere and in 2 rats in the right hemisphere. Occipital cortex was the first EEG lead at which the signs appeared. In frontal cortex epileptic activity started later, (569-1188 s after the moment of penicillin administration) and it began from precipitating of the sleep spindles, which were changed into spikes and waves. At the height of these bursts of activity interictal spikes were observed.

First ictal signs were observed in 16-122 min from the moment of administration of penicillin, and during 6 h of observation from 2 up to 20 ictal periods of activity were registered in control group of rats. The duration of intervals between ictal discharges was from 2 up to 50 min.

Epileptic activity in the brain structures was present during six h from the moment of administration (313,2±14,9 min).

The dynamics of the amplitude of the ECoG was characterized by an increase till the 80-th min of observation after penicillin administration. The average amplitude during this period was between 1200-1600 mcV. Afterwards, from 100 till 240th min after administration, a relatively stable period was observed. A decline of the amplitude was the final stage of observation and base-levels were reached at approximately 340 min after injection.

1.2. Mathematical modeling of the evolution of the generalized epilepsy.

The equations of multiple linear regression which reflects connections between indices which were under investigation - the amplitude of seizure potentials as recorded during the first hour of observation were the next:

$$YA4k=(57{,}00\pm64{,}46)+(-0{,}28\pm0{,}096)*A1k\#+(0{,}84\pm0{,}09)*A2k\#+(0{,}10\pm0{,}088)*A3k \quad R^2=0{,}5926,\ T=8{,}36,\ \text{Residual dispersion } 225{,}37 \qquad (1.1)$$

$$YA1k=(149{,}12\pm29{,}12)*\#+(-0{,}13\pm0{,}063)*A4k\#+(0{,}29\pm0{,}061)*A2k\#+(0{,}69\pm0{,}059)*A3k \quad R^2=0{,}7962,\ T=13{,}69,\ \text{Residual dispersion}=153{,}023 \qquad (1.2)$$

$$YA2k=(110{,}51\pm55{,}88)*\#+(0{,}48\pm0{,}083)*A1k\#+(0{,}63\pm0{,}079)*A4k\#+(-0{,}062\pm0{,}076)*A3k \quad R^2=0{,}7071,\ T=10{,}76,\ \text{Residual dispersion}=195{,}36 \qquad (1.3)$$

$$YA3k=(-122{,}30\pm51{,}68)*\#+(0{,}96\pm0{,}076)*A1k\#+(-0{,}053\pm0{,}072)*A2k+(0{,}065\pm0{,}073)*A4k \quad R^2=0{,}7606,\ T=12{,}35,\ \text{Residual dispersion}=180{,}69 \qquad (1.4)$$

The equations of multiple linear regression which describes connections between indices, which were under investigation during the second hour of investigation, were the next:

$$YA4k=(786{,}79\pm68{,}30)+(-0{,}14\pm0{,}062)*A1k\#+(0{,}59\pm0{,}10)*A2k\#+(-0{,}63\pm0{,}091)*A3k \quad R^2=0{,}5639\ T=6{,}53,\ \text{Residual dispersion}=157{,}87 \qquad (1.5)$$

$$YA1k=(-181{,}23\pm83{,}18)*\#+(-0{,}12\pm0{,}11)*A4k\#+(0{,}46\pm0{,}097)*A2k\#+(1{,}03\pm0{,}085)*A3k \quad R^2=0{,}8895\ T=16{,}29,\ \text{Residual dispersion}=146{,}22 \qquad (1.6)$$

$$YA2k=(2{,}61\pm62{,}96)*\#+(0{,}46\pm0{,}058)*A1k\#+(0{,}51\pm0{,}11)*A4k\#+(-0{,}19\pm0{,}084)*A3k \quad R^2=0{,}6908\ T=8{,}59,\ \text{Residual dispersion}=145{,}55 \qquad (1.7)$$

$$YA3k=(-375{,}31\pm44{,}78)*\#+(0{,}52\pm0{,}041)*A1k\#+(-0{,}097\pm0{,}068)*A2k+(-0{,}27\pm0{,}075)*A4k \quad R^2=0{,}8819\ T=15{,}70,\ \text{Residual dispersion}=103{,}49 \qquad (1.8)$$

The third hour of observation was characterized by the next equations:

$$YA4k=(258{,}38\pm88{,}00)+(-0{,}45\pm0{,}079)*A1k\#+(0{,}026\pm0{,}09)*A2k\#+(-0{,}31\pm0{,}079)*A3k \quad R^2=0{,}7721\ T=6{,}64,\ \text{Residual dispersion}=60{,}86 \qquad (1.9)$$

YA1k=(-172,96±98,12)*#+(0,97±0,19)*A4k#+(0,53±0,14)*A2k#+(0,29±0,12)*A3k
R^2=0,8242 T=7,81, Residual dispersion=89,33 (1.10)

YA2k=(153,66±143,31)*#+(0,65±0,13)*A1k#+(0,069±0,22)*A4k#+(0,081±0,13)*A3k
R^2=0,6924 T=5,41, Residual dispersion=99,11 (1.11)

YA3k=(768,12±205,09)*#+(0,46±0,85)*A1k#+(0,67±0,01)*A2k+(-1,04±0,85)*A4k
R^2=0,5504 T=3,98, Residual dispersion=141,38 (1.12)

Equations for the fourth hour of observation:

YA4k=(453,18±131,39)+(0,95±0,15)*A1k#+(-1,42±0,12)*A2k#+(0,76±0,086)*A3k
R^2=0,7771 T=6,99, Residual dispersion=62,09 (1.13)

YA1k=(-182,26±55,45)*#+(0,70±0,11)*A4k#+(1,22±0,103)*A2k#+(-0,60±0,07)*A3k
R^2=0,7803 T=7,05, Residual dispersion=53,51 (1.14)

YA2k=(292,27±80,22)*#+(0,61±0,088)*A1k#+(-0,53±0,08)*A4k#+(0,52±0,05)*A3k
R^2=0,9249 T=13,14, Residual dispersion=37,91 (1.15)

YA3k=(-437,07±143,47)*#+(-0,96±0,16)*A1k#+(1,66±0,13)*A2k+(0,91±0,14)*A4k
R^2=0,8756 T=9,93, Residual dispersion= 67,81 (1.16)

Equations for the fifth hour of observation:

YA4k=(44,43±95,21)+(0,75±0,13)*A1k#+(0,15±0,07)*A2k#+(-0,57±0,13)*A3k
R^2=0,6901 T=5,97, Residual dispersion=70,58 (1.17)

YA1k=(140,77±45,19)*#+(0,42±0,10)*A4k#+(0,17±0,051)*A2k#+(0,49± 0,099)*A3k
R^2=0,8577 T=9,82, Residual dispersion=52,77 (1.18)

YA2k=(-288,24±181,23)*#+(1,12±0,24)*A1k#+(0,56±0,26)*A4k#+(0,15±0,25)*A3k
R^2=0,7345 T=6,65, Residual dispersion=134,36 (1.19)

YA3k=(58,48±100,82)*#+(0,98±0,13)*A1k#+(0,94±0,071)*A2k+(-0,63±0,15)*A4k
R^2=0,6800 T=5,83, Residual dispersion=74,74 (1.20)

Last hour used for the analysis was described by the next number of equations:

YA4k=(-42,35±46,96)+(0,33±0,11)*A1k#+(0,065±0,10)*A2k#+(0,45±0,12)*A3k
R^2=0,6607 T=6,84, Residual dispersion=134,46 (1.21)

YA1k=(50,50±22,32)*#+(0,13±0,07)*A4k#+(0,66±0,06)*A2k#+(0,13±0,07)*A3k
R^2=0,8773 T=13,11, Residual dispersion=83,65 (1.22)

YA2k=(-7,95±36,95)*#+(1,05±0,09)*A1k#+(0,039±0,09)*A4k#+(-0,04±0,09)*A3k
R^2=0,8491 T=11,62, Residual dispersion=105,81 (1.23)

YA3k=(37,25±50,88)*#+(0,41±0,12)*A1k#+(-0,083±0,11)*A2k+(0,53±0,13)*A4k
R^2=0,6225 T=6,29, Residual dispersion=145,68 (1.24)

Note: # - significant value of coefficient of regression, which later on was depicted with proper lines in multigrafs.
With * multiplication is marked.

In Fig.1 the multicycling multigraphs are presented. They illustrate per- hour evolution of relationships between seizure potentials generated in different regions of brain. In other words, these multigraphs interpret in geometrical form number of equations, which are pertinent to the approximation of the amplitudes earlier.

During the first hour of observation mutually positive influences were determined between left and right hemispheres and between left hemisphere and frontal cortex, while negative ones were registered when relationships between left hemisphere and occipital cortex were analyzed (Fig.1, A). Mutually positive influences were determined between right hemisphere and occipital cortex during first two hours of observation as well (Fig.1, A, and B). It should be stressed that only mutually positive influences between left and right hemispheres

were those ones which preserved during all the period of EEG registration, while similar relationships (mutually positive) between left hemisphere and frontal cortex were timely (4th hour, Fig. 1, D) substituted by negative ones.

Second and third hours of observation were characterized by the establishment of mutually negative influences between frontal and occipital cortex, and preservation of those ones left hemisphere and occipital cortex were pertinent for the third hour of observation (Fig 1, C).

Mutually positive influences between left hemisphere from one side, right hemisphere and occipital cortex from other, as well as between frontal cortex from one side and right hemisphere and occipital cortex from other were observed during fourth hour of observation (Fig. 1, D). Besides, negative influences between right hemisphere and occipital cortex along with negative influences between left hemisphere established during first hour between left hemisphere from one sides and right hemisphere and frontal cortex from the other (Fig.1, B, C). Besides, negative effects of left hemisphere upon occipital cortex and positive one from frontal cortex upon right hemisphere were noted during second hour (Fig.1, B), while positive influences between and frontal cortex were registered as well. It should be noted that the residue variance was minimal this period of time.

Fifth hour of observation was characterized by the same picture of relationships as it was determined during third hour of observation (Fig.1, E). The difference between 5^{th} and 6^{th} (final stage) hours of observation was confined to substitution of mutually negative influences between frontal and occipital cortex by negative ones (Fig. 1,F).

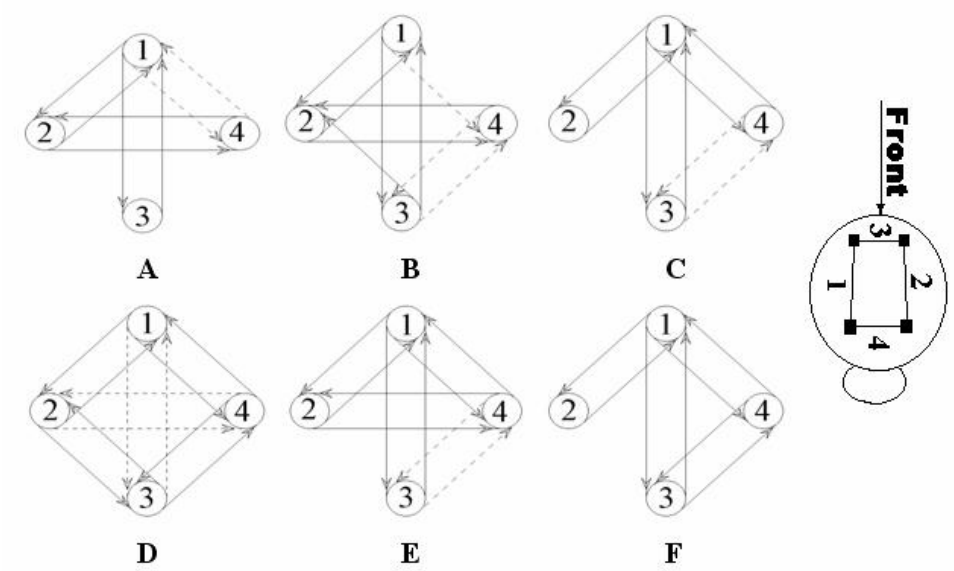

Fig. 1. Policycle multigraphs representing results of multiple linear analysis of average amplitude of signals in different cortical leads in Wistar rats with generalized epileptic syndrome.
Notes: A-, B-, C-, D-, E-, and F- 1-t, 2-d, 3-th, 4-th, 5-th and 6-th hours from the moment of benzilpenicillin solution (300,000 IU/100 g) i.p. administration to Wistar rats.
1 - left hemisphere, 3 - right hemisphere, 3 - frontal and 4 - occipital bipolar leads.
Solid line- positive influence, and interrupted line- negative influence, with arrows the directions of influences are marked.

#2. Absence epilepsy in WAG/rij rats.

For the investigations of spike-wave activity of WAG/rij rats the periods of these bursts were collected and altogether artificially 220 sec period was composed, which served for the further multiple linear regression analysis. The typical form of bursts of spikes and waves are presented at Fig. 2. It should be noted that all episodes were taken when rats demonstrate passive wakefulness behavior.

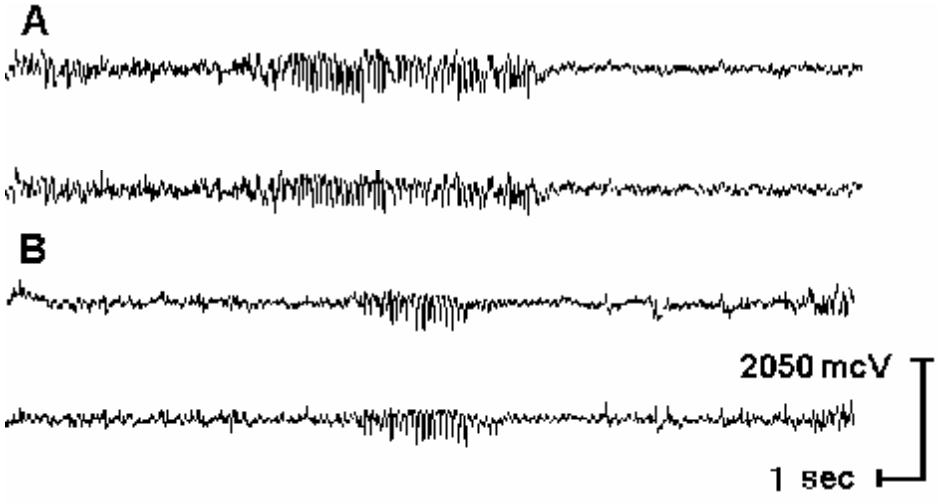

Fig. 2. ECoG of WAG/rij rat registered bipolarly and used for the consequent multiple linear analysis.
A - left (upper lead), and right (second lead) hemispheres, B - frontal (upper lead), and occipital (second lead) cortex.
Seconds are marked at the bottom of figure.

Policycle multigraf presentation of data revealed the net prevalence of positive influences between all structures, which were under investigations (Fig. 3). The apparent exception were relationships between left hemispheral cortex and frontal cortex, where negative directed to frontal leads influence was present. This effect might be regarded as the indirect positive relationships between left hemispheral cortex and frontal leads (cortex), which might be realized via both right and occipital cortical zones (in accordance to rules of path-way analysis, which is accepted for operations on policycle multigrafs). Meanwhile, direct influences from from left cortex to frontal cortical zones were characterized by negative sign.

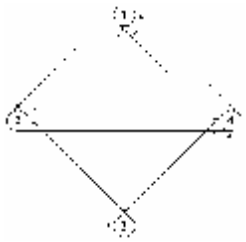

Fig. 3. Policycle multigraph representing results of multiple linear analysis of average amplitude of signals in different cortical leads in WAG/rij rats suffering from absence epileptic syndrome.
Notes: the same as in Fig.1.

Hence, obtained data revealed that during the evolution of generalized penicillin-induced epileptiform activity specific relations between different zones of brain cortex might be observed. Most frequently (most stable) were effects of the involvement of left hemisphere into formation of mutually positive influences with right hemisphere and frontal cortex, while first two hours of the epileptic activity development were characterized by negative influences of left hemisphere upon occipital cortex. It is also of worth to note that significant influences upon other cortical zones were most numerous from left hemisphere.

Most frequently negative influences upon other cortical zones were generated by occipital cortex: such ones were noted during first 5 hours of observation upon one of other cortical zones. Negative influences from frontal cortex upon occipital one were also noted on 2-d, 3-d, and 5^{th} hours of observation.

It is also of interest to note that influences between frontal cortex and right hemisphere were least numerous, while influences (mutually positive ones) between frontal cortex and left hemisphere were observed during all the period of observation with the exception on 4^{th} h when they were substituted by negative ones.

Hence, most generally for the development of penicillin-induced generalized seizure activity the prevalence of positive influences in comparison with the negative ones between structures is quite characteristic. The decreasing of residual variance observed in the time – course of epileptic activity development with the least value on 4^{th} h of observation might be hallmark for the high level of interconnections between zones which are under investigation

[5]. Indeed, the number of actual (significant) interrelations is maximal during this period of time.

How gained data might correspond to the well known neurophysiological peculiarities of generalized epileptiform activity, induced by penicillin administration?

As far as we dealt with penicillin-induced seizures, role of frontal (motor) cortex is of interest. Hence, this cortex was most stable with respect to creation of mutually positive influences with left hemisphere - the only exception was on 4^{th} h when they were substituted by negative ones, but this period was characterized by establishment of mutually positive influences with right hemisphere, and it should be stressed that this period was the only one when such relationships between frontal and right hemispheral cortex were created. These peculiarities might be in favor for the leading (dominant) role played by left hemispheral cortex in the process of recruitment of frontal cortex in generation of epileptiform manifestations. Just only short period (4^{th} h) was characterized by substitution of this driving function of left hemisphere on the driving role of right hemisphere.

It should be noted that drives from left hemispheral cortex (or other zones) upon frontal cortex might be mediated via right hemishperal cortex or occipital one (Fig 1,D) in accordance of path-way analysis of policycle multigrafs [5].

Taking into consideration that left hemisphere was supposed to be more epileptogenic [3] in comparison with other brain zones which were under investigation, more divergent ("branched") character of relations between left hemisphere and their cortical zones is in good correspondence with this notion. Thus, based on our data showing most numerous powerful influences between left hemisphere and the rest cortical zones, left hemispheral cortex might regarded as most prone to be involved into eileptogenesis as well as most "expansive" with regrad to the involvement of other cortical zones. Opposite to this, occipital cortex might be regarded as least prone to be involved into the entire system encompassed by positive influences, and, even more, are able to counteract to such recruitment.

Such an explanation of observed phenomena might be of worth for the correspondence between definition "positive influence" and "spreading of epileptiform activity". Vice versa, negative influences reflects opposite situation when such spreading is not happened. It is important to note that the identification of relations as negative influences does not mean "inhibition" of epileptiform activity in one structure by influences from other one. It is sooner that dynamic relationships between amplitudes of epileptic discharges is opposite one and resultant amplitudes/power of epileptogenesis might be well comparable with that one observed during period of positive influences registration.

That is why terms "excitation" and inhibition" are not proper in all cases for the analysis with proposed method. Such a conclusion is in good correspondance with the final stage of epileptogenesis development (6^{th} h), which was the only period when negative influences are completely lost. Hence, suppression of penicillin-induced epileptogenesis was followed by the net prevalence of positive influences between structures, which were under investigation. The prevalence of the total number positive interrelationships during second half of observation (starting from the 4^{th} h up to 6^{th} h) over that one observed during first 3 h also is in favor for the significance of positive influence as marks of processes of declining of epileptiform activity.

It should be noted that this late stage of epileptiform activity development when actual concentration of penicillin decreased, might be in correspondence with the absence type of seizures to some extent. Such an analogue is possible to be made because of low concentrations of benzilpenicillin, which are able to induce subtle excitation of cortical inhibitory interneurons, but fail to break down inhibition lead to precipitation of spike-wave discharges [4]. Taking into consideration the only difference between generalized "seizure" and absence types of penicillin epilepsy confined to the presence or absence of significant negative influences, it might be supposed that absence type of epilepsy is characterized by net prevalence of positive influences between cortical zones.

This suggestion partially was supported by investigations on WAG/rij rats, which are regarded as typical form of absence epilepsy [2, 7, 9]. Hence, these observations clearly showed that the net difference between grand mal and petit mal might be confined to the prevalence of mutually positive interactions between different zones of brain cortex, which encompassed almost all of them. Meanwhile, relatively stable relations between left hemispheral cortex and frontal cortex (bipolar interhemispheral leads), which were observed during 5 h out of 6 h after penicillin administration, were the apparent exception in case of absence epileptic activity in WAG/rij rats. Both in case of grand mal and petit mal we have observed stable relations between left and right hemispheres. Least stable in grand mal epilepsy were between right cortex

and frontal cortex, which were represented in the form of positive relationships in WAG/ rij rats.

Thus, observed prevalence of positive relationships between cortical structures in course of spike-wave activity generation might be in favor for the synchronous involvement of all inspected cortical areas into shifting of amplitudes of all registered signals/discharges. This feature, which was pertinent for WAG/rij rats, was quite in difference when compared with generalized seizures in Wistar rats. Thus, for the generalized seizure activity the stable character of positive relations was seen only for interhemispheral interaction, while the rest of the cortical zones were involved into such form of interaction on less stable basis.

It should be noted that some notions on the brain asymmetry might be derived from both investigations on Wistar and WAG/rij rats. Hence, during 6-th hour of generalized penicillin epilepsy development the obvious absence of connections between frontal cortex and right hemispheral cortex as well as between right hemispheral and occipital one were registered. Meanwhile, in WAG/rij rats the only absence of relations between left hemisphere and frontal cortex was in favor of some form of “lateralization” of interhemispheral relationships. Hence, interhemispheral relations might be inspected and informative with regard to both generalized and absence epilepsies manifestations.

In conclusion it should be noted that presentation of data of multiple linear analysis is of interest for the comparison with other forms of EEG data presentation, which are made most widely as special color "maps". Those maps are more dynamic, but policycle multigrafs also might cover different including “real time” periods of EEG observation. Besides, clear sense of terms "positive-, negative influence" along with statistics procedures might serve for quick and reliable definition of all the picture of brain working. This aspect of used method is very representative for the observation of effects of neurotropic compounds and identification of their mode of action.

Perspectives of multigraf presentations of the multiple linear regression analysis of EEG data are connected with the further development of mathematical apparatus, which is able to perform specific operations with multigrafs per se.

REFERENCES

1. Azen R., Budescu D.V. // Psychol.Methods. - 2003. - Vol. 8. - № 2. - P. 129-148.
2. Coenen A.M.L., Drinkenburg W.H.I.M., Inoue M. van Luijtelaar E.L.J.M. // Epilepsy Res. - 1992. - Vol. 12. - P. 75-86.
3. Godlevsky L.S., van Luijtelaar E.L.J.M., Shandra A.A., et. al. // Medical Hypotheses. - 2002.- Vol. 58. - P. 237-243.
4. Gloor P. // Epilepsia. - 1990. - Vol. 20. - № 4. - P. 571-588.
5. Lobasyuk B.A. The analysis of neurophysiological mechanisms of cessation of multifocal cortical epilepsy // Thesis PhD. – Novosibirsk. - 1988. - 202 p.
6. Manheim J.B., Rich R.K. Politology. Methods of investigations (translation from English with an introduction after Sokoloff A.K.). Moscow: Mir Publisher. - 1997. - 544 p.
7. Meeren H.K.M., van Luijtelaar E.L.J.M., Lopes de Silva F.H., et. al. // Uspehi Fiziologicheskih Nauk (Moscow). - 2004. - Vol. 35. - P. 3-19.
8. Paxinos G. Watson C. The Rat Brain in Stereotaxic Coordinates, Academic Press Inc., Sydney. - 1998.
9. Van Luijtelaar E.L.J.M. Coenen A.M.L. // Neurosci. Lett. - 1986. - Vol. 70. - P. 393-397.