BIOMETRICS

Secular rhythms and Halberg's paraseasonality in the time occurrence of cerebral stroke

Kovac M, Mikulecky M Sn

*Clinic of Neurology, Faculty of St. Ladislaus, Nové Zámky, Slovakia.***kovacm@nspnz.sk**
*Studenohorska Street 2071, Bratislava, Slovakia.***statistics@nel.edu**

Abstract

Objectives: **To obtain the optimal information concerning the time course of the morbidity od cerebral stroke.**
Background: **Recently, long years' cycling, similar to that in sun and geomagnetic activity, is observed in various biomedical variables. Other discovery is that of transyear (over one year) and cisyear (under one year) rhythms,originating also in the sun, in medicine.**
Subjects: **There were 6100 patients with cerebral infarction, 415 with intracerebral and 277 with subarachnoid hemorrhage admitted at Clinic of Neurology in Nové Zámky (area with 70 km radius and 180 000 inhabitants). Their monthly numbers were registered since January 1989 up to December 2004.**
Methods: **The data were processed by Halberg's cosinor regression. Presence of linear trend and of the period lengths of 10.5 (solar Schwabe-cycle), 5.25, 7.04 (geomagnetic activity cycling), 3.52, 1.70, 1.50, 1.30 (solar wind cycling), 1.20, 1.00 and 0.50 years was tested. Level of statistical significance was set at alpha=0.05.**
Results: **In all three time series, significant linear trends were found with the estimated monthly increase by 0.8 % of the estimated starting mesor value for infarction, 1.2 % for cerebral and 1.9 % for subarachnoid hemorrhage. Both the solar and geomagnetic cycling with their second harmonics were significant in all three clinical diagnoses. The transyear with period length of 1.3 year was significant in both hemorrhages while in infarction only its borderline significance was achieved. Nevertheless, its amplitude was always higher (by 15 to 83 %) than that of 1.00 year estimated cosinusoid.**
Conclusion: **All presented time series document increasing trends in the morbidity on cerebral stroke in the given geographic area. The presence of secular, years lasting cycles adds to relatively long list of similar chronocosmoepidemiologic analyses, so far generally ignored due to insufficient understanding of inferential statistics and chronobiology among doctors. The transyear paraseasonality represents a new element in these studies. To honour the nestor of the world chronobiology, who highly acknowledged the work of Ladislav Dérer, the designation "Halberg's paraseasonality" is proposed *(Tab. 2, Fig. 3, Ref. 17)*.**
Key words: cerebral stroke, south-west Slovakia, 16 years, hospital admissions, solar activity, geomagnetic activity, transyear, inferential statistics.

The Medline search of the published analyses (http://gateway.ut.ovid.com/gw2/ ovidweb/cgi) of secular, i.e. years lasting rhythms on one side and of paraseasonal cycles close to but significantly differing from one year on the other shows increasing frequency of the former, and quite recently the emergence of the latter.

Thus, for example, the „periods of 7 and/or 10 years" were mentioned in Ovid/OLDMEDLINE and MEDLINE in 1950–2005 23-times, the term "circadecadal" 7-times (2000–2003),

Clinic of Neurology, Faculty of St. Ladislaus, Nové Zámky, Slovakia

Address for correspondence: M. Kovac, Clinic of Neurology, Faculty of St. Ladislaus, Slovenska 11/A, SK-940 34 Nove Zamky, Slovakia. Phone: +421.35.6912626

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Dedication: The paper is dedicated to the blessed memory of Assoc. Prof. RNDr. Dipl. Ing. L. Kubackova, DSc, the outstanding Slovak mathematical statistician.

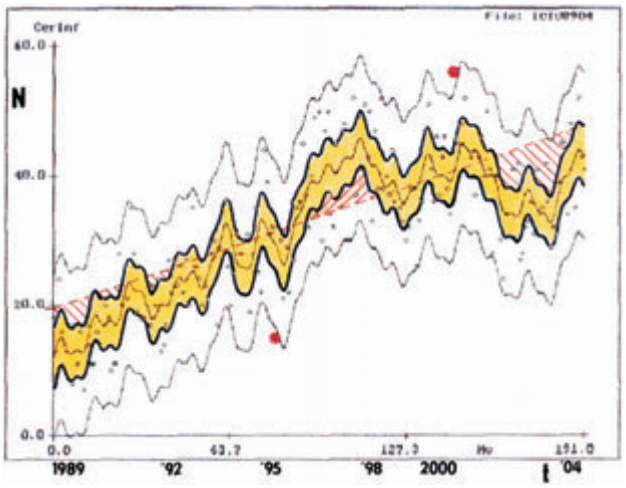

Fig. 1. Monthly numbers (N, ordinate, dots) of cases of cerebral infarction in the defined geographical area, observed since January 1989 to December 2004, plotted versus time in months (t). Also some calendar years are shown.The dashed straight line indicates the linear trend. Upper and lower limit of 95 % confidence corridor is shown by bold lines, parallel upper and lower 95 % tolerance limits by thin lines. Two large heavy dots correspond with 95 % tolerance outliers. Non-overlapping of the trend straight line by the confidence corridor is shadowed and marks significant up or down deviations.

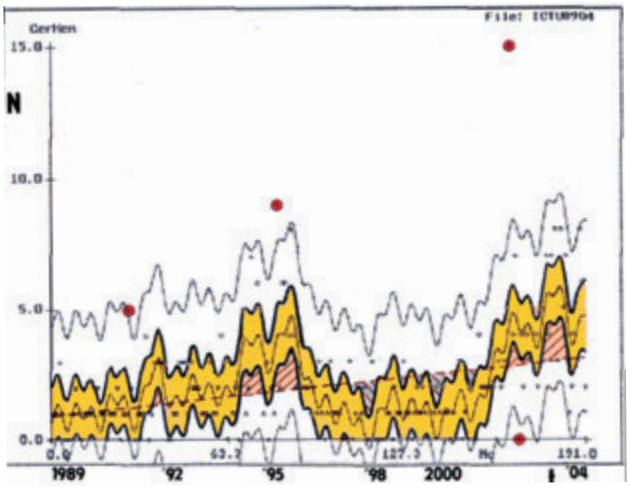

Fig. 2. Analogy of Fig. 1 for cerebral hemorrhage, with 4 tolerance outliers.

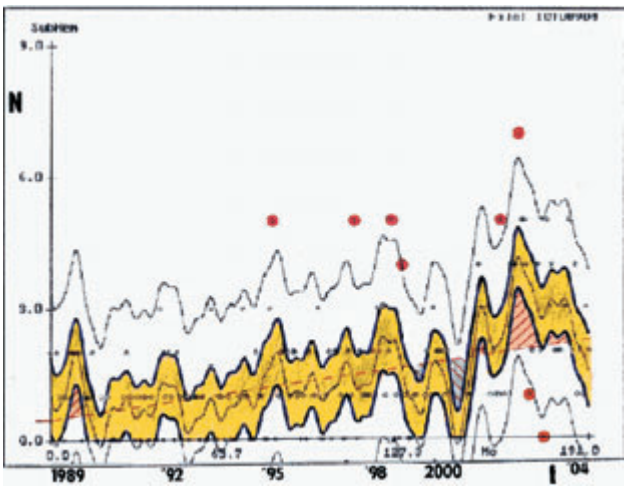

Fig. 3. Analogy of Fig. 1 for subarachnoid hemorrhage, with 8 tolerance outliers.

the term “Hale” (21 years) and/or “Schwabe” (about 10 years) “cycle” 3-times (2001–2003) and the term “circaseptennian” 7-times (1987–1998). As to the “transyear”, so far only one title was published (in 2003).

Our group around the Biometry Unit of the Ist Medical Clinic, Comenius University, was oriented on developing the chronobiologic legacy of Academician Dérer. The Unit has been de facto closed on December 31, 2004 by decision of the new management of the united Teaching Hospital Bratislava. In the rise of annual numbers of human larval toxocariasis in Slovakia, 7-years-periodicity was described in the year 1992 (1). One year later, 7- and 12-years rhythms with their harmonics were identified in echinococcosis of swines and sheep (2). The 10-years periodicity dominated in long years’ time series of abortions of young girls in Slovak as well as in Czech Republic (3). Such studies in humans started a few years later also abroad, as far as we know, particularly in USA and Japan (e.g. 4, 5). Also 21-years’ (Hale) cycles were discovered, e.g. in the numbers of published papers related to toxocariasis (6) and in psychic phenomena (7).

Interestingly, similar periods were described also for animals and plants. Thus, a circaseptennian, i.e. about 7-yearly rhythm has been found in gonadal weight of marine invertebrates (8). In chronobotany, a 2189-years series of averages of ring measurements on 11 sequoia trees displays components with periods of about 10.5 and 21 years, similar to the Schwabe- and Hale- cycles of solar activity (9).

Recently, another rhythm coming putatively from the sun is that of the “transyear”, i.e. with the period length e.g. of 1.3 year. This periodicity, present in the solar wind speed, was discovered in blood pressure measurements (10).

Subjects

Monthly numbers (the data file is available at the Email address of either author) from the total of 6100 patients with cerebral infarction, 415 with intracerebral and 277 with subarachnoid hemorrhage, altogether of 6792 patients admitted at Clinic of Neurology in Nové Zámky between January 1, 1989 and December 31, 2004 are scrutinized. The source area of the Clinic has the radius of approximately 70 km with 180 000 inhabitants.

Cerebral infarction was caused by thrombosis of extracranial arteries, with possible embolization into intracerebral arterial stream, or by primary thrombosis of intracranial arteries. The intracerebral hemorrhage occurred usually within an acute blood pressure increase under presence of atherosclerotic changes in intracerebral arteries. The underlying causes for the subarach-

Tab. 1. Parameter estimates for cerebral infarction (CerInf, Fig. 1), cerebral hemorrhage (CerHem, Fig. 2) and subarachnoid hemorrhage (SubHem, Fig. 3). The point and 95 % confidence (in brackets) estimates of the regression parameters are given.

	CerInf	CerHem	SubHem
Mesor	19 (17; 21)	1,0 (0,4;1,5)	0,5 (0,1-0,8)
Linear trend	+0,15***	+0,011***	+0,009***
	(+0,13;+0,17)	(+0,006;+0,016)	(+0,006;+0,012)
CD	0,737	0,439	0,277
PERIODS:			
10,5y Amp	6,6***(5,2;8,0)	1,6***(1,1;2,0)	0,37**(0,11;0,63)
Acro	Aug97	Jan94	Feb91
	(Mar97;Dec97)	(Aug93;Jun94)	(Dec89;May92)
5,25y Amp	2,9***(1,5;4,2)	0,57*(0,12;1,01)	0,45**(0,16;0,74)
Acro	Dec91	Jan90	Jun93
	(Jun91;Jun92)	(May89;Aug90)	(Dec92;Dec93)
7,04y Amp	3,9***(2,5;5,2)	0,81***(0,43;1,19)	0,72***(0,46;0,99)
Acro	May93	Mar90	Apr89
	(Nov92;Nov93)	(Jul89;Nov90)	(Okt88;Okt89)
3,52y Amp	2,8***(1,5;4,1)	0,66***(0,30;1,02)	0,40**(0,17;0,64)
Acro	Okt90	Jun92	Mar92
	(Jul90;Jan91)	(Feb92;Sep92)	(Nov91;Jun92)
1,70y Amp	NS	NS	NS
1,50y Amp	NS	NS	NS
1,30y Amp	NS	038*(0,03-0,74)	0,38**(0,15-0,61)
Acro	-	Sep89	Jan90
		(Jul89;Dec89)	(Nov89;Feb90)
1,20y Amp	NS	NS	0,32**(0,10;0,65)
Acro	-	-	Okt89
			(Aug89;Dec89)
1,00y Amp	NS	NS	NS
0,50y Amp	NS	0,39*(0,05;0,74)	NS
Acro	-	Apr89	-
		(Apr89;May89)	
	*P≤0,05	**P≤0,01	***P≤0,001

CD = coefficient of determination, y = year, Ampl = amplitude, Acro = acrophase, NS = nonsignificant. * p≤0.05, ** p≤0.01, *** p≤0.001. The calendar dates are truncated

noid hemorrhage were inborn or acquired arterial aneurysms or inborn arteriovenous malformations.

The available up-to-date diagnostic procedures included computed tomography (CT) of brain, CT-angiography, ultrasonography of extra- and intracranial arteries, magnetic resonance imaging (MRI) of brain and MRI-angiography.

Methods

The obtained monthly frequencies were plotted versus corresponding months of the total of 192 months, equal to 16 years. These data were evaluated by Halberg's cosinor regression (11) using original computer programme (12). Presence of linear trend and of the period lengths of 10.5 (solar Schwabe-cycle), 5.25 (its second harmonics), 7.04 (leading period of geomagnetic activity cycling), 3.52 (its second harmonics), 1.70, 1.50, 1.30 (solar wind cycling), 1.20, 1.00 (the yearly seasonal rhythm) and 0.50 (the semiannual rhythm) years was tested on the level of statistical significance set at alpha=0.05 and with 170 degrees of freedom, derived from 192 measurements minus 22 estimated parameters, i.e. mesor, linear trend and 10 periodic components, each with its amplitude and acrophase. Results will be expressed on one side as the parameters' point and 95 % confidence estimates, and on the other graphically as the total approximating function with the 95 % confidence and 95 % tolerance corridors. The parameters include the mesor – the middle value of the rhythm, for equidistant measurements (as in the present work) identical with their arithmetic mean; the linear regression coeffi-

cient expressing the estimated increment of monthly number of cases per one month; the amplitude of rhythm and its acrophase for 10 periodic components; acrophase shows the first estimated peak after the time equal zero, i.e. after January 1989. Also the coefficient of determination is calculated: it is equal to the square of the correlation coefficient, in the present setting nonlinear, and denotes the proportion of the total variance explained by the regression. In other words, it expresses the quality of the regression.

The ratio of amplitudes for the 1.5 and 1.3 year's rhythm to that of the circaannual rhythm was also calculated in each diagnosis. The global result was evaluated by the sign test, based on the binomial distribution.

Results

The chronograms – graphical display showing the measurements and their regression approximation – are reproduced in Figs 1, 2 and 3.

In Table 1, the most important numerical results are shown for each of the three diagnoses.

The ratios of amplitudes for transannual and circaannual cyclings are given in Table 2. The uniformly lower amplitude of circaannual cycling is statistically significant.

The numbers of 95 % tolerance outliers, i.e. of the measurements outside of the corridor of 95 % tolerance, are appropriate, being in each diagnosis under 100–95 % = under 5 % of 192 measurements, i.e.under nine.

Discussion

In all three time series, significant linear trends were found with the estimated monthly increase by 0.8 % of the estimated starting mesor value for infarction, by 1.2 % for cerebral and by 1.9 % for subarachnoid hemorrhage. Both the solar 10.5 years' and geomagnetic 7.04 years' cycling with their second harmonics were significant in all three clinical diagnoses. The transyear with period length of 1.3 year was significant in both hemorrhages while for infarction only its borderline significance was achieved. Nevertheless, its amplitude was always significantly higher (by 15 to 83 %) than that of the circaannual estimated cosinusoid.

The found and discussed periods are known to astronomers and geophysicists from the studies of sun and geomagnetic activity. One of the leading periods of the latter is for example given as 7.04 years (13). It is possible that such variables will in future be monitored from the point of view of prevention of diseases states. That' s why we tried to calculate the prognosis of sun activity, measured as the Wolf numbers, i.e. solar spots' numbers up to the year 2040 (14).

Conclusion

All presented time series are documenting the increasing trends in the morbidity on cerebral ictus in the given geographic area. This is, from the point of view of clinical medicine and epidemiology of stroke, the most important and actual finding. The present paper does not address the issue of the causal nexus responsible for this phenomenon. One of the reasons could be aging of the population, another one a more stressful life of today. No worsening of medical services is considered: an opposite appears true. Nevertheless, it seems paradoxical that the incidence of these cerebral complications of arterial hypertension, hyperlipidemia and atherosclerosis is rising while the niveau of antihypertensive and antihyperlipidemic therapy as well as that of prevention with anticoagulants improves. The real cause can be the inappropriate way of living of people relying on better medical care and some broadly advertised preventive measures.

Tab. 2. Ratio of amplitudes for selected period lengths in the three diagnoses.

	CerInf	CerHem	SubHem
Ampl 1.5 year/1.0 year	1.18	1.11	1.01
Ampl 1.3 year/1.0 year	1.15	1.18	1.83

The presence of secular, years lasting cycles is no surprise. It adds to relatively long list of similar chronocosmoepidemiologic analyses, so far generally ignored. This ignorance is partly explained by insufficient understanding of the principles of inferential statistics among doctors. Particularly the inferential, not a merely descriptive way of biometrical evaluation towards obtaining the optimal information and towards decision making is substantial. Its knowledge, however, is minimal, not only among medical doctors. The used approach is based on the original Slovak contributions in this field (15, 16).

The transyear paraseasonality represents a quite new element in these studies. To honour the nestor of the world chronobiology, who highly acknowledged the work of Academician Ladislav Dérer (17), designation "the *Halberg's paraseasonality*" is proposed.

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