INCREASE IN STROKE DEATHS AFTER 1997 IN THE CZECH REPUBLIC

FIŠER B.¹, CORNÉLISSEN G.⁴, SIEGELOVÁ J.², DUŠEK J.², HOMOLKA P.², MAZÁNKOVÁ V.³, HALBERG F.⁴

¹Ministry of Health, Prague, ²Department of Functional Diagnostic and Rehabilitation, Faculty of Medicine, St. Anne's Teaching Hospital, Masaryk University, Brno, and ³Institute of Medical Information, Prague, Czech Republic; ⁴Halberg Chronobiology Center, University of Minnesota, Minneapolis, MN, USA

Abstract

Yearly mortality data on stroke in the Czech Republic, recorded from 1950 to 1999, were analysed. About 50- and 21-year cycles were suggested, regardless of whether all data were considered or whether they were analysed for men and women separately. After detrending, a self-starting cumulative sum (CUSUM) control chart showed an increase in stroke deaths that took place around 1997. These results are in keeping with similar findings in four other geographic locations. They warrant a renewed effort toward stroke prevention. Ambulatory monitoring of blood pressure and heart rate in the general population is a useful tool to detect and correct certain abnormalities of the circadian pattern of these variables which have been associated with large increases in stroke risk, even in conventionally normotensive subjects.

Key words

Stroke, Yearly mortality, Czech Republic

INTRODUCTION

Morbidity and mortality from stroke and other cardiovascular events have long been shown to follow non-random circadian and circannual patterns (1-12). Most of the epidemiological studies reveal a morning peak at the onset of stroke and its higher occurrence in winter than in summer in temperate regions. About-weekly and half-weekly patterns in stroke incidence have also been documented (11, 13-21). Differences in timing have been reported in relation to different disease aetiologies (14). For instance, the incidence of strokes associated with subarachnoidal haemorrhage differs in its circadian and circaseptan timing from that of lacunar infarctions and other kinds of strokes (14). The incidence of strokes associated with a cardiac embolus also differs in its circannual timing from that of strokes associated with large vessel disease (14). In general, strokes tend to occur preferentially on Mondays (13).

Mortality from myocardial infarction in Minnesota has also been shown to undergo an about 10.5-year cycle, similar to the solar activity cycle (22, 23).

During years of maximal solar activity, there is an excess of 220 myocardial infarction deaths per year as compared to years of minimal solar activity, representing a 5% change in mortality (22, 23). This study investigates whether long-term changes also characterise stroke deaths in the Czech Republic.

MATERIALS AND METHODS

Yearly mortality from stroke in the Czech Republic was recorded from 1950 to 1999. Only total mortality data were analysed, in view of changes in disease classification during the span covered, and not deaths in subcategories such as subarachnoid vs. intracerebral haemorrhage or occlusion of cerebral arteries. The data on overall mortality and for each gender separately were analysed by least-squares spectra (24), with frequencies in the range of one to 11 cycles per 52.5 years. The choice of the fundamental period, slightly longer than the observation span, stems from the desirability to include a trial period of 10.5 years, the average solar cycle length for the span under study. In view of a prominent about 50-year cycle, analyses were repeated on the residuals from this long-term trend and from a third-order polynomial. Components corresponding to spectral peaks were further assessed by nonlinear rhythmometry (24,25,26).

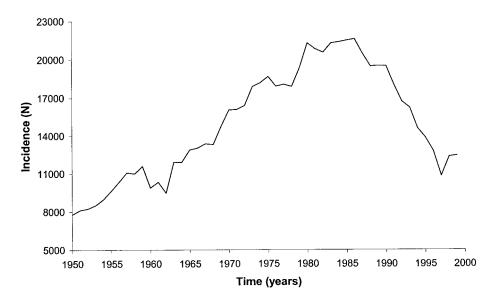
RESULTS

The time course of stroke deaths is illustrated in *Fig. 1*. A prominent about 50-year cycle was validated nonlinearly (*Table 1*). After removing this major component, an about 21-year cycle was suggested, but reached only borderline statistical significance (*Table 1*). In view of the non-sinusoidal waveform of the about 50-year cycle, a third-order polynomial was fitted to the data. Residuals, shown in *Fig. 2*, were analysed by self-starting CUSUM, a control chart procedure (*27*). When the last 8 years were considered, an increase in stroke deaths was detected in 1999. From these data it is derived that stroke mortality increased from 1997 to 1999.

DISCUSSION

With the qualification that there have been changes in the classification of mortality from stroke, a non-monotonic trend over the past 50 years has been documented both in the Czech Republic and in Minnesota (23, 28). This result raises the question whether the decline in stroke during the past two decades cannot be accounted for, at least in part, by a natural about 50-year cycle. Of course, one should not use 50 years of data to discuss an about 50-year periodicity (29), unless there is collateral evidence. The historical case of Mark Beaufoy, an artillery colonel who provided data for one cycle before Samuel Heinrich Schwabe's discovery of the sunspot cycle, is illustrative. Beaufoy's data permitted the documentation in geomagnetics of the same cycle length that was found subsequently in sunspots (30, 31) and was further confirmed for the Schwabe cycle (32) in a perspective of centuries.

In the case of a recent increasing trend in stroke deaths, there is corroborating evidence from other studies. An upward trend in stroke mortality has been

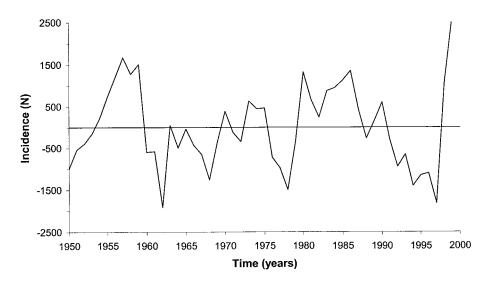


 $\label{eq:Fig.1} \textit{Fig. 1}$ Incidence of strokes in the Czech Republic (1950–1999).

 $\label{eq:Table 1} Table \ 1$ Nonlinear estimation of about 50- and 21-year cycles in stroke mortality

Data set	Period (years)	Double amplitude (N)
	(95% confidence interval)	
Original data:		
Men	53.3 (49.4; 57.9)	46.1 (39.9; 52.3)
Women	55.0 (51.3; 59.4)	71.3 (62.9; 79.8)
All	54.3 (50.6; 58.7)	117.3 (102.9; 131.8)
Residuals from about 50-year cycle:		
Men	21.3 (17.1; 27.4)	15.1 (1.7; 28.4)*
Women	21.4 (16.8; 27.9)	22.5 (1.7; 43.2)*
All	21.4 (17.0; 27.7)	37.5 (3.5; 71.5)*
	. , ,	` ' '

^{*}One-parameter limits (lower limit of nonlinear interval overlaps zero).



 $Fig.\ 2$ Stroke incidence in the Czech Republic. Residuals from the third order of a polymonial.

observed in most recent years not only in the Czech Republic and in Minnesota, but also in Slovakia (33), Lund, Sweden (34), and Arkansas (28).

While treatment and public education are very important to limit the incidence of strokes, the decrease seen after 1985 may not only be a response to changes in patient management but may also, at least in part, represent a response to environmental influences characterised by very-low-frequency components, such as a circasemicentennial cycle that needs replications not only in different geographic locations but also over several longitudinal cycles before qualifying as a rhythm. The recent identification of an excessive circadian blood pressure amplitude, as well as of a deficit in heart rate variability, as independent additive features of a risk syndrome for stroke and other vascular morbidity (22, 35), should prompt systematic monitoring of the population. Since conditions of altered variability can be transient (36), a minimal 7-day monitoring is recommended for screening. The implementation of this task is facilitated by an offer, made by the industry, of a 90% decrease in the cost of ambulatory blood pressure monitors for participants in the BIOCOS project that aims at stroke prevention. The Ministry of Health of the Czech Republic fully endorses this goal that is now implemented, as the routine 7-day monitoring of blood pressure and heart rate, at St. Anne's Teaching Hospital of Masaryk University in Brno.

Acknowledgements

This study was supported by U.S. Public Health Service (GM-13981; FH); Dr. h.c. Dr. h.c. Earl Bakken Fund (FH, GC); University of Minnesota Supercomputing Institute (FH, GC) and by the grant J037/98:141100004 (Czech Ministry of Education).

Fišer B., Cornélissen G., Siegelová J., Dušek J., Homolka P., Mazánková V., Halberg F.

ZVÝŠENÍ POČTU ÚMRTÍ NA CÉVNÍ MOZKOVOU PŘÍHODU PO ROCE 1997 V ČESKÉ REPUBLICE

Souhrn

Byly analyzovány údaje o roční mortalitě v důsledku mrtvice v České republice zaznamenávané od roku 1950 do roku 1999. Uvádějí se cykly v délce trvání asi 50 a 21 let, ať jsou uvažovány všechny údaje nebo jsou analyzovány samostatně pro muže a ženy. Kolem roku 1997 došlo ke zvýšení počtu úmrtí na mrtvici. Tyto výsledky jsou v souladu s podobnými nálezy ve čtyřech jiných zeměpisných lokalitách a zdůvodňují obnovenou snahu o prevenci mrtvice. Ambulantní monitorování krevního tlaku a srdeční frekvence u široké veřejnosti je užitečné pro zjišťování a nápravu určitých abnormalit cirkadiánního průběhu těchto proměnných, které byly spojovány s výrazným zvýšením rizika mrtvice i u normotenzivních osob.

REFERENCES

- 1. Bock KD, Kreuzenbeck W. Spontaneous blood pressure variations in hypertension, the effect of antihypertensive therapy and correlations with the incidence of complications. In: Gross F, ed. Principles and Practice: An International Symposium. New York: Springer-Verlag, 1966:
- 2. Smolensky M, Halberg F, Sargent F Chronobiology of the life sequence. In: Itoh S, Ogata K,
- Yoshimura H, eds. Advances in Climatic Physiology. Tokyo: Igaku Shoin Ltd., 1972: 281–318.

 3. Reinberg A, Gervais P, Halberg F et al. Mortalité des adultes: Rythmes circadiens et circannuels dans un hôpital parisien et en France. Nouv Presse méd 1973; 2: 289–294.
- Myers A, Dewar HA. Circumstances attending 100 sudden deaths from coronary artery disease with coroner's necropsies. Brit Heart J 1975; 37: 1133–1143.
 Agnoli A, Manfredi M, Mossuto L, Piccinelli A. Rapport entre les rythmes héméronyctaux de la
- tension artérielle et sa pathogénie de l'insuffisance vasculaire cérébrale. Rev Neurol 1975; 131: 597-606.
- 6. Marler JR, Price TR, Clark GL. Morning increase in onset of ischemic stroke. Stroke 1989; 20: 473-476.
- 7. Marshall J. Diurnal variation in occurrence of strokes. Stroke 1977; 8: 230–231.
- Tsementzis SA, Gill JS, Hitchcock ER, Gill SK, Beevers DG. Diurnal variation of and activity during the onset of stroke. Neurosurgery 1985; 17: 901–904.
 Muller JE, Tofler GH, Stone PH. Circadian variation and triggers of onset of acute cardiovascular disease. Circulation 1989; 79: 733–743.
 Manfredini R, Squarzoni G, Gallerani M, Franceschini F, Bariani L, Fersini C. Temporal
- organization of cerebrovascular accidents: a retrospective, preliminary study about stroke in Ferrara, Italy. Rivista Europea per le Scienze Mediche e Farmacologiche 1990; 12: 223–228.
- Pasqualetti P, Natali G, Casale R, Colantonio D. Epidemiological chronorisk of stroke. Acta neurologica scandinavica 1990; 81: 71–74.
 Gallerani M, Manfredini R, Ricci L. Chronobiological aspects of acute cerebrovascular diseases.
- Acta Neurol Scand 1993; 87: 482-487.
- Cornélissen G, Breus TK, Bingham C et al. Beyond circadian chronorisk: worldwide circaseptan-circasemiseptan patterns of myocardial infarctions, other vascular events, and emergencies. Chronobiologia 1993; 20: 87–115.
 Johansson BB, Norrving B, Widner H, Wu J, Halberg F. Stroke incidence: circadian and circaseptan (about-weekly) variations in onset. Prog Clin Biol Res 1990; 341A: 427–436.
- 15. Feigin VL, Anderson CS, Anderson NE et al. Is there a temporal pattern in the occurrence of subarachnoid hemorrhage in the southern hemisphere? Pooled data from 3 large, population-based incidence studies in Australia, 1981 to 1997. Stroke 2001; 32: 613–619.

- 16. Nicolau GY, Haus E, Popescu M, Sackett-Lundeen L, Petrescu E. Circadian, weekly, and seasonal variations in cardiac mortality, blood pressure, and catecholamine excretion. Chronobiol Int 1991; 8: 149–159.
- 17. Manfredini R, Gallerani M, Portaluppi F, Salmi R, Fersini C. Chronobiological patterns of onset of acute cerebrovascular diseases. Thromb Res 1997; 88: 451–463.
- 18. Pasqualetti P, Colantonio D, Casale R, Acitelli P, Natali G. Cronobiologia della morte cardiaca improvvisa. Evidenza di una periodicita circadiana, circasettana e circannuale nella sua incidenza [The chronobiology of sudden cardiac death. The evidence for a circadian, circaseptimanal and circannual periodicity in its incidence]. Minerva Med 1990; 81: 391–398.
- 19. Willich SN, Lowell H, Lewis M, Hormann A, Arntz HR, Keil U. Weekly variation of acute myocardial infarction. Increased Monday risk in the working population. Circulation 1994; 90:
- 20. Spielberg C, Falkenhahn D, Willich SN, Wegscheider K, Voller H. Circadian, day-of-week, and seasonal variability in myocardial infarction: comparison between working and retired patients.
- Seasonal variability in flipocardial infarction: comparison between working and retired patients. Am Heart J 1996; 132: 579–585.
 21. Arntz HR, Willich SN, Schreiber C et al.. Diurnal, weekly and seasonal variation of sudden death. Population-based analysis of 24,061 consecutive cases. Eur Heart J 2000; 21: 315–320.
 22. Cornélissen G, Halberg F, Schwartzkopff O et al. Chronomes, time structures, for chronobioengineering for "a full life". Biomed Instrum Technol 1999; 33: 152–187.
 23. Cornélissen G, Halberg F, Breus T et al. Non-photic solar associations of heart rate variability and myocardial infarction. J Atmospheric Solar-Terrestrial Physics (in press).
 24. Cornélissen G, Halberg F, Chronomedicine, In: Armitage P, Colton T, eds. Encyclopedia of

- Cornélissen G, Halberg F. Chronomedicine. In: Armitage P, Colton T. eds. Encyclopedia of Biostatistics, Vol. 1. Chichester, UK: John Wiley & Sons Ltd., 1998: 642–649.
- 25. Marquardt DW. An algorithm for least-squares estimation of nonlinear parameters. J Soc Indust Appl Math 1963; 11: 431–441.
- 26. Rummel JA, Lee JK, Halberg F. Combined linear-nonlinear chronobiologic windows by least–squares resolve neighboring components in a physiologic rhythm spectrum. In: Ferin M, Halberg F, Richart RM, Vande Wiele R, eds. Biorhythms and Human Reproduction, Int. Inst. for the Study of Human Reproduction Conference. Proc. New York: John Wiley & Sons, 1974:
- 27. Hawkins DM. Self-starting CUSUM charts for location and scale. Statistician 1987; 36: 299-315.
- 28. Halberg F, Cornélissen G, Otsuka K et al. Cross-spectrally coherent ~10.5- and 21-year biological and physical cycles, magnetic storms and myocardial infarctions. Neuroendocrinol Lett 2000; 21: 233–258.
- 29. *Malin S.* Historical introduction to geomagnetism. In: Jacobs JA, ed. Geomagnetism, Vol. 1. London: Academic Press, 1987: 1–25.
- 30. Schwartzkopff O, Cornelissen G, Bingham C et al. Long-term, when-needed lifelong monitoring concerns governments, ethics committees and everybody. In: Halberg F, Kenner T, Fiser B, eds. Proceedings, Symposium: The Importance of Chronobiology in Diagnosing and Therapy of Internal Diseases. Faculty of Medicine, Masaryk University, Brno, Czech Republic, January 10–13, 2002. Brno: Masaryk University, 2002: 97–121.
- 31. Schwabe H. Über die Flecken der Sonne. Astronomische Nachrichten 1838; 15: 244–248
- 32. Schwabe H. Sonnen-Beobachtungen im Jahre 1843. Astronomische Nachrichten 1844; 21:
- Kovac M, Mikulecky M. Chronocosmobiology of cerebral stroke in south west Slovakia. Proceedings 1st International Symposium, Workshop on Chronoastrobiology & Chronotherapy (Satellite Symposium, 7th Annual Meeting, Japanese Society for Chronobiology), Kudan, Chiyodaku, Tokyo, 11 Nov 2000, p. 56.
- 34. Johansson Björn, Norrving B, Lindgren A. Increased stroke incidence in Lund-Orup, Sweden, between 1983 to 1985 and 1993 to 1995. Stroke 2000; 31: 481–486.
- 35. Halberg F, Cornélissen G, Halberg J et al. Circadian Hyper-Amplitude-Tension, CHAT: a disease risk syndrome of anti-aging medicine. J Anti-Aging Med 1998; 1: 239–259.
 36. Halberg F, Cornélissen G, International Womb-to-Tomb Chronome Initiative Group.
- Resolution from a meeting of the International Society for Research on Civilization Diseases and the Environment (New SIRMCE Confederation), Brussels, Belgium, March 17–18, 1995: Fairy Tale or Reality? Medtronic Chronobiology Seminar No. 8, April 1995, 30 pp.