Материалы
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«ИНТЕГРАЦИЯ НАУКИ И ПРАКТИКИ: ИТОГИ, ДОСТИЖЕНИЯ И ПЕРСПЕКТИВЫ»

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«The next set of abstracts is an outgrowth of activities started by Denis Gubin in Minnesota, years ago, and signals the resumption of international cooperation in Tyumen, within the project on the biosphere and the cosmos, BIOCOS, in the steps of Alexander Leonidovich Chijevskiy and Vladimir Ivanovich Vernadsky, to both of whom, along with Gennady Gubin, this section is dedicated».

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INTERMITTENT MILD VASCULAR VARIABILITY ANOMALIES (VVAS), A CHALLENGE FOR THE OVERALL POPULATION AND CARE PROVIDERS

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In the presence or absence of high blood pressure, VVAs are associated with an increased cardiovascular disease risk, as documented in several outcome studies. They can occur in patients treated for hypertension, sometimes as a consequence of medications taken to lower blood pressure, if treatment is administered at an inappropriate circadian stage. VVAs can be no more than a response to an emotional, physiological, or other load. If they persist in consecutive 7-day ABPM records analyzed chronobiologically (C-ABPM), however, they become Vascular Variability Disorders (VVDs), and merit treatment in their own right. VVAs involve deviations in one or several characteristics of the circadian patterns in blood pressure and/or heart rate from those of clinically healthy peers, matched by gender and age. The circadian characteristics are estimated by cosinor, a regression method consisting of the least squares fit of cosine curves to the data collected around the clock. Because abnormal patterns can occasionally occur in relation to a load («stress») and can be affected by the kind, dose and timing of medication, continuous surveillance is recommended as a means to monitor health. Lifestyle adjustments can be made in response to monitoring, and can help one to avoid or better cope with external loads, such as emotions. One VVA is MESOR-hypertension (MH), diagnosed as an elevation of the blood pressure MESOR (Midline Estimating Statistic Of Rhythm), a rhythm-adjusted mean, usually more accurate and more precise than the arithmetic mean. A circadian overswing (CHAT, brief for Circadian Hyper-Amplitude-Tension, defined as too large a circadian amplitude of blood pressure) is another VVA. Other VVAs include an excessive pulse pressure and an excessive pulse pressure product, deficient heart rate variability, ecphasia (an odd phase of circadian rhythm of blood pressure but not of heart rate), and ecfrequentia (statistically significant deviation from 24 hours of the circadian period of blood pressure and/or heart rate). In one clinical trial, CHAT was associated with an increase in the risk of a cerebral ischemic event within 6 years that is double the risk associated with MH. Even in the absence of MH, CHAT is associated with a statistically significant increase in risk.

Herein, we report on the results from 9 consecutive weeks of C-ABPM by a husband-and-wife team. While the wife (CL) had a consistently acceptable chronobiologic summary (referred to as a sphygmochron; 1), her husband (CG) had one or several VVAs in several weekly summaries. CG had been hospitalized and had surgery for a hemorrhagic stroke in 2007, about 5.5 years prior to the monitoring. He had mostly recovered in the interim. CHAT was detected in his first two weekly records but not in the next three or in the 7th and 8th profiles, which showed acceptable blood pressure patterns. CHAT recurred in the 6th and 9th week. Diastolic MH was also present in the last 3 profiles but not in the first 6. Deficient heart rate variability (too low a standard deviation of heart rate) was also occasionally found (during weeks 1, 2, 6, 7, and 9). The treating physician, a busy nephrologist, was informed by telephone after the second week of monitoring. Should the patient wait until the next scheduled appointment in another month? During the first week, the double 24-hour amplitude of systolic blood pressure was 41.6 mmHg when the upper limit of acceptability is 34 mmHg. Except for week 7 when it dropped below 25 mmHg, the double 24-hour amplitude of systolic blood pressure remained above 30 mmHg. In the last week, it was 37.3 mmHg, involving a relatively small elevation of only 3 mmHg above the upper limit of acceptability.

The question is now one of ethics: current business plans for physicians have no reward for optimizing the personalized timing of administration of anti-hypertensive medication, based on C-ABPM. Changing the treatment time was shown for some patients to eliminate CHAT while the same dose of the same drug combination given to the same patient exacerbated CHAT when given at another circadian stage. A consensus document, signed by two physiologists, both department heads, one the late Bohumil Fiser, former minister of health of the Czech Republic and a member of the Board of the World Health Organization, the other Thomas Kenner, former president of the University of Graz, Austria, advocated the implementation of measures to eliminate VVAs. We can only record the status quo, but were unable to influence those who wrote the last guidelines, much evidence notwithstanding beyond the consensus (1, cf. 2-9).

CL, who prompted CG to monitor, is completing a master's degree. Her thesis deals with a method for the diagnosis of CHAT and for following its time course. Graphic displays can readily be interpreted by the patient. The suite of R programs should become freely accessible on the internet, as are analyses at this time from corne001@umn.edu. We look for any and all opportunity to report a case which is probably not unusual. The technology exists to continuously monitor pressure in car tires or in the blood of very small rodents (to develop hypotensive drugs). C-ABPM is available for human use as well, but current medical practice does not screen for VVAs. Thus far, MH is the only VVA physicians check for, and all too often only as office spotchecks during infrequent office visits, despite the known limitations of such sporadic measurements, and despite the fact that in one study CHAT is associated with twice the risk of an adverse outcome within 6 years, as compared to MH. CHAT is detected in over 5% of the subjects monitored in several different geographic locations worldwide. It thus affects a very large patient population that could benefit from the C-ABPM approach as a guideline for personalized timed treatment. The US Center for Disease Control (CDC) regards blood pressure as enemy No.2, smoking being identified as the enemy No.1 (10, cf. 11). The World Health Organization has described non-communicable diseases such as those associated with high blood pressure as a slow moving disaster (12). An affordable, unobtrusive chronobiologically-interpreted ABPM, could be implemented on a large scale, perhaps via a cloud system, operated via a website (1). Such education and pre-habilitation could prevent the need for costly hospital stays, lengthy rehabilitation, and extended human suffering. Governments and/or insurers might investigate this as a potential cost saving measure, given the large number of people affected by high blood pressure, and the growing population of elderly.

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CHRONOBIOLOGICALLY-INTERPRETED AMBULATORY BLOOD PRESSURE MONITORING (C-ABPM) OF SHIFT-WORKERS IN SIBERIA

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C-ABPM in several outcome studies in Minnesota, the Czech Republic, Germany, Japan and Taiwan has shown that in addition to an elevated blood pressure (BP), abnormal variability patterns of BP and heart rate (HR), usually not routinely screened for in conventional practice, are also associated with an increased cardiovascular disease risk (1). These abnormalities are referred to as Vascular Variability Anomalies (VVAs), or, if they persist, as Vascular Variability Disorders (VVDs) (1). They are diagnosed by sphygmochron (2), a computer summary of a double-barreled approach consisting of a parametric and non-parametric assessment of data collected around the clock, preferably for a minimum of 7 days. Parametrically, a 2-component model consisting of cosine curves with periods of 24 and 12 hours is fitted by least squares to the data to yield estimates of the MESOR (Midline Estimating Statistic Of Rhythm, a rhythm-adjusted mean value, usually more accurate and more precise than the arithmetic mean), double amplitude (a measure of the predictable extent of change within a cycle) and acrophase (a measure of the timing of overall high values recurring in each cycle) of each component. Non-parametrically, the percent time elevation, amount of excess and timing of largest excess are estimated by numerical integration in comparing the subject's average 24-hour profile obtained by stacking the data along an idealized day with time-specified 90% prediction limits qualified by gender and age. VVAs are detected when estimates of the 24-hour cosine curve in the composite model exceed the upper 95% prediction limit of clinically healthy peers matched by gender and age. VVAs include MESOR-hypertension, EPP (Excessive Pulse Pressure, when the difference in MESOR between systolic and diastolic BP exceeds 60 mmHg), CHAT (Circadian Hyper-Amplitude-Tension, an excessive circadian amplitude of BP), ecphasia (odd timing of the circadian rhythm of BP but not of HR), ecfrequentia (statistically significant deviation from 24 hours of the circadian period of BP and/or HR), DHRV (Deficient HR variability, when the standard deviation of HR is below 7.5 beats/min), and EPPP (Excessive Pulse Pressure Product, when the SBP x HR product (/100) exceeds 100) (3). As a dividend, C-ABPM data have proven useful to learn about influences from the environment, near and far, on human cardiovascular physiology (4). Herein, we examine a database of 24-hour ABPM records from presumably normotensive male subjects, 29-58 years of age, engaged in monthly rotational shift work in Tyumen Far North (Yamburg station, 68° N).

Each subject provided a 24-hour ABPM record on 5 or 6 different occasions, in consecutive seasons. The data were analyzed by sphygmochron (5) to identify VVAs. For systolic (S), mean arterial (MA) and diastolic (D) BP and HR, the standard deviation (SD), MESOR (M), 24-hour amplitude (A), and corresponding percentage rhythm (PR, the proportion of overall variance accounted for by the 24-hour cosine curve fitted to the data) of each subject's record was expressed as a percentage of all profiles contributed by him. These relative values were pooled across all 129 subjects and assigned to the date of monitoring (between July 2006 and February 2011). These newly formed time series were analyzed by least squares spectra in the frequency range of 1 cycle in 5 years to 15 cycles per year, complemented by the extended nonlinear cosinor to estimate the period with its 95% confidence interval (CI), using Marquardt's algorithm (6). As subjects came from different locations varying between 2611 and 3458 miles from the geomagnetic North Pole, circadian rhythm parameters were compared among the different sites by 1-way analysis of variance (ANOVA) and linear regression analysis.

By comparison with clinically healthy peers matched by gender and age, the following VVAs were identified. There were 8 records from 6 subjects with systolic MESOR-hypertension, and 25 records from 18 subjects with diastolic MESOR-hypertension. Systolic and diastolic MESOR-hypotension was found in 3 records from 3 different workers and in 1 record from a single worker, respectively. EPP was found in only one record. Systolic CHAT occurred in 5 records from 5 different subjects, and diastolic CHAT in 5 records from 4 different subjects, indicating that CHAT may have been transient, perhaps related to the work load, rather than persistent. Systolic and diastolic ecphasia found in 37 and 30 records, respectively, may have been related to shift-work. The records being limited mostly to about 24 hours, they were too short to test for ecfrequentia. A higher-than-expected number of records (123/659 or 18,7%) from 75 workers has a PPP above 100, while in another 207 records, the PPP is between 90 and 100, a level already associated with a statistically significant increase in cardiovascular disease risk in one outcome study. DHRV is also detected in a larger-than-expected number of records, namely in 95 records (14,4%) from 62 subjects (48,1%, at least part of the time).

Least squares spectra of longitudinal series of pooled relative endpoints reveal the presence of peaks corresponding to periods longer than 1 year, whereas no spectral peak is observed at precisely 1 year. Table 1 summarizes the results by listing the largest peak detected in the para-annual region of the spectrum, and the overall largest peak, whether it was anticipated or not. Amplitude ratios (in %) in Table 1 also compare these amplitudes and that of an anticipated 1.32-year component (corresponding to a signature of the solar wind, found in all BP and HR longitudinal records available for analysis thus far; 7, 8) to the amplitude of the calendar year. While it is not surprising that amplitudes of spectral peaks are larger than the 1.0-year amplitude, the about 1.32-year (transyear) tends to be more prominent than the calendar year as well, Table 1. In the case of DBP, nonlinear analyses confirm the presence of a statistically significant transyear for the overall SD, and for the 24-hour amplitude and its corresponding PR. Period estimates [and their CIs] are for DBP-SD 1.75 [1.45, 2.04] years, for DBP-A 1.30 [1.08, 1.53], and for DBP-PR 1.31 [1.07, 1.54] years, with corresponding amplitudes (in %) of 4.9 [1.7, 8.1], 9.0 [1.2, 16.8], and 12.7 [1.2, 24.2], respectively.

Linear regression analyses do not find any relationship of MESORs or circadian amplitudes as a function of distance from the magnetic North Pole. By ANOVA, regional differences are found for the MESOR of SBP (p<0,001), MAP (p<0,001), and DBP (p=0,002), but not for the circadian amplitudes (p>0.40). As a group, the BP MESORs are higher for subjects in Moscow (55°45'N, 37°37'E) and Ufa (54°49'N 56°4'E) than for subjects in Tyumen (57°10'N 65°30'E) and regional territories (not more distant than 300 km) and in Krasnodar (45°2'N 38°58' E).

One major lesson learned from this study is the dominance of para-annual components over the calendar-yearly variation associated with the changing of the seasons in a region with large fluctuations in both temperature and day length between winter and summer. Of particular interest is the detection of a transyear modulating the circadian amplitude of DBP, in keeping with results documented in longitudinal (rather than hybrid) records (7, 8). Another

Table 1

Endpoint	Para-Annual Peak			Overall largest peak			Period = 1.32y		Period = 1y		A-Ratios		
	Period	Amplitude		Period	Amplitude		Amplitude		Amplitude		ParaA/1y	Largest/1y	1.32y/1.0y
SBP-SD	1.786	4.916	ss	1.786	4.916	ss	1.788	ns	1.379	ns	356.490	356.490	129.659
SBP-PR	0.532	8.070	ss	0.142	8.184	ss	4.129	ns	3.446	ns	234.185	237.493	119.820
SBP-M	2.083	0.954	ss	2.083	0.954	ss	0.529	ss	0.278	ns	343.165	343.165	190.288
SBP-A	0.781	4.638	ns	0.154	5.483	ss	1.739	ns	2.390	ns	194.059	229.414	72.762
MAP-SD	1.923	4.731	ss	1.923	4.731	ss	1.711	ns	2.492	ns	189.848	189.848	68.660
MAP-PR	0.532	12.350	ss	0.532	12.350	ss	6.606	ns	4.404	ns	280.427	280.427	150.000
MAP-M	1.923	0.561	ss	0.305	0.663	ss	0.345	ns	0.333	ns	168.468	199.099	103.604
MAP-A	0.833	6.126	ss	0.163	6.322	ss	5.695	bs	1.824	ns	335.855	346.601	312.226
DBP-SD	1.786	4.847	ss	1.786	4.847	ss	2.508	bs	1.950	ns	248.564	248.564	128.615
DBP-PR	1.316	12.714	ss	0.142	14.318	ss	12.714	ss	4.517	ns	281.470	316.980	281.470
DBP-M	1.087	0.486	ns	0.152	0.857	ss	0.396	ns	0.465	ns	104.516	184.301	85.161
DBP-A	1.316	9.013	ss	1.316	9.013	ss	9.013	ss	1.130	ns	797.611	797.611	797.611
HR-SD	3.125	6.158	ss	0.263	6.503	ss	1.183	ns	1.194	ns	515.745	544.640	99.079
HR-PR	2.778	19.323	ss	2.778	19.323	ss	1.703	ns	4.064	ns	475.468	475.468	41.905
HR-M	3.125	2.734	ss	3.125	2.734	ss	0.338	ns	0.427	ns	640.281	640.281	79.157
HR-A	2.273	8.085	ss	0.212	8.291	ss	0.949	ns	0.427	ns	1893.443	1941.686	222.248

SBP: Systolic Blood Pressure; MAP: Mean Arterial Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; SD: Standard Deviation; M: MESOR; A: 24-hour Amplitude; PR: Percentage Rhythm of 24-hour component; y: year; ss: Statistically Significant (P<0.05); ns: Not statistically significant (P>0.05); P-values from zero-amplitude (no rhythm) test, not corrected for multiple testing. Amplitude ratios are expressed in %.

important finding is the larger-than-expected number of abnormalities in the pulse pressure product and heart rate variability of this population. Whether these VVAs are associated with the monthly rotational shift work these subjects are engaged in, or whether they relate to their geographic location as it may be affected by terrestrial and space weather remains to be determined. In any event, the identification of VVAs in 5 to 6 records in consecutive seasons from 129 shift-workers has laid the foundation for determining their ability to predict actual adverse cardiovascular outcomes, should it be possible to follow-up on their health status, preferably with repeated weeklong monitoring, as recommended in a consensus document (1).

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MULTIDECADAL CYCLES IN ONTOGENY QUALIFY VASCULAR VARIABILITY ANOMALIES (VVAS) DEFINED TRANSVERSELY FROM CLINICAL TRIALS

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This abstract, with direct clinical implications, is dedicated to Gennady Gubin (1), since, on so-far uniquely long (and relatively dense) data, it reveals cycles in ontogeny, a topic in which Gennady had great interest from a circadian viewpoint, to be extended to infradians. Vascular Variability Anomalies (VVAs) or Disorders (VVDs) (2, 3) were formulated on the basis of (the then only available) transverse time series (with outcomes), as yet limited in density and length. Hence, the values at which a given marker variable used for diagnosis (such as a blood pressure) may be regarded as anomalous, are tentative, until they can be viewed in the light of longitudinal scarce reference values. For example, VVAs include the Pulse x systolic blood Pressure Product (/100) (PPP), considered excessive when its value exceeds 90 mmHg x beats/minute. This limit was based on results of several clinical transverse trials on populations, with each individual studied around the clock at most for a few days. These derived transverse population limits must be personalized as decades-long (eventually life-long) records from clinically healthy long-lived subjects may become available (4). The need for revision and qualification is apparent from a 44.5-year record of a clinically healthy man (RBS). Four to six measurements were available during wakefulness on most days, with a large spread around two fitted models apparent in their plot. Individual measurements fluctuate above as well as below the (population) limit of acceptability of 90 (mmHg x beats/min)/100. A multi-component, realistic model, with several ups and downs, has a point estimate of the period (τ) of 46.79 years with a CI (95% confidence interval) of 41.94 to 51.64 years, covering a τ of 50 years. A single component model fitted to the same data has a shorter τ with a CI overlapping, at its longer end, the CI of the multi-component model. If one does not have the preceding decades-long record, a clinically healthy low-risk man may be misdiagnosed as being at a high risk of severe vascular disease. From an applied clinical viewpoint, this is a strong argument for advocating self-surveillance starting as early as possible, preferably at birth but not later than at middle-school age.

On the basic side, long periods may be considered as physiologic counterparts of Kondratiev cycles between 40 and 60 years, already reported in economics by Hyde Clarke (5) 166 years ago, or perhaps of a Brьckner-Egeson-Lockyer (BEL) cycle (6-8; cf. 9-11), defined as approaching, with the CI of its τ, the 30-40-year range (12). Whatever the definitive length may turn out to be (should RBS' record lengthen and be analyzed), in an economic series, a 30-40-year and a 40-60-year spectral component coexisted in the same data, as is the case in RBS for different variables, changing in τ with the length of the series, a circumstance qualifying changes with age. A unified science is interdisciplinarily cross-validating and, in the case of human aging, replications of putative 50-year cardiovascular cycles are more readily feasible transversely in anthropometry (13) and in economics (12) than in scarce centenarians (14). Shorter than decadal infradian solar signatures, such as trans-years or weeks, have been shown to persist in the cardiovascular system, albeit damped, when their counterparts are no longer detected in the environment (15, 16). Moreover, decadal and multidecadal periods in the blood circulation can free-run from putative external counterparts (15, 16). Accordingly, genetic coding of decadal cycles can also be anticipated. We need to clarify genetically coded mechanisms involved in multidecadals, as in other infradians (17), as compared to those now mapped chronobiologically and molecularly for the circadian cardiovascular system (18). Be that as it may, the putative long cyclic variation in PPP, just like that found in RBS in systolic blood pressure, among other variables and subjects (16), are all to be considered for the diagnosis of cardiovascular disease risk. This goal can be implemented by chronobiologically interpreted life-time ambulatory blood pressure monitoring (C-ABPM), now feasible and less demanding than the self-surveillance practiced by RBS.

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WRIST ACTIVITY OF 9 ELDERS: SEMIANNUAL, TRANSANNUAL, BUT NO ANNUAL SPECTRAL COMPONENT, MAGNETISM REPLACING SEASONALITY

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Beyond assessing sleep patterns and daily activity (1; cf. 2-5), actigraphy can focus on infradian rhythms, scrutinizing annual vs. para-annual behavior, thus attempting to gauge the relative contributions to human well-being of helio- and/or geomagnetism, on the one hand versus other aspects of terrestrial climate and weather (6-9). This can be done by computing cosinor spectra (10) extended nonlinearly by Marquardt's algorithm (11) and comparing the amplitude, A, of a calendar-yearly (seasonally, photically, thermically and societally) synchronized circannual rhythm of a given biospheric time series – that has a CI (95% confidence interval) of its period, τ, covering 365 days – versus the A of a semiannual component, associated prominently with geomagnetism, that has a CI of τ covering 0.5 year and versus the As of any components that have a para-annual and/or para-semiannual τ, whose CI overlaps neither the 1.0- nor the 0.5-year length but are near these lengths, within limits still to be defined as data accumulate.

This approach was implemented by unobtrusively recorded wrist activity of 6 subjects ranging from 60 to 95 years of age (1), by telemetry in a facility for assisted living in Finland and of 3 clinically healthy, independently living subjects in Minnesota (12, 13). The relative brevity of the series obtained on 9 subjects (3 investigators, 6 patients), with records of at least 9 months up to ~2 or ~3 years in the patients, restricts the finding of a nonlinearly validated transyear of 1.190 years (y) with a CI extending from 1.015 to 1.315 y in a single subject (13), while in the other patient, with a record of ~2-years, a linear estimate shows a peak at 1.1 years, none at a τ at 1.0 year. In all 9 subjects, to whatever the length of their series permits, a calendar-yearly component could not be demonstrated.

Transyears originate in sunspots as noted by Stetson who referred to them as a "secondary fluctuation" (14). They are gauged in solar wind speed (15, 16) and in the biosphere (8; cf. 7). In 3 of the patients in Finland, there was a spectral component with a CI of τ overlapping 0.5 year.

While, as noted, 3 subjects in Minnesota, 92, 89 and 61 years of age at the start of years-long monitoring, also showed no circannual component, by contrast to the Finns, no semiannual component was seen in the 3 Minnesotans. There was a cis-half-year (or quinmensal component, with a period of about 5 months) with an estimated τ of ~0.45, 0.42 and 0.41 y, with CIs not overlapping 0.5 year. All 3 Minnesotans, able to care for themselves, showed a likely signature of solar flares (17, 18).

In summary, 3 of 6 elderly residents in an assisted-living facility in Finland had putative signatures of terrestrial magnetism (half-yearly spectral components). The failure to detect a calendar-yearly component, to whatever extent the small sample sizes of 6 and 3 (total of 9) subjects in Finland and Minnesota permit, could be interpreted as being in keeping with the assumption that human elderly's well-being may be influenced by magnetism more than by any effect of the seasons (if the latter is at all present). In both of two Finnish residents with appropriately long records, a transyear was found, validated nonlinearly in only one of them, as a putative signature of heliomagnetism. The second subject, with a 2-year record, showed a transyear in a linear analysis. In all three Minnesotans, a quinmensal was found, a putative signature of heliomagnetism.

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PERSONALIZED CHRONOUSPHERES (CHRONO-NOOSPHERES): TEMPORO-SPATIALLY GLOBAL AND LOCAL

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As a young scholar in history, Alexander Leonidovich Chijevskiy recognized the need for meta-analyses of time series in history. He undertook this task with his unaided eye in the pre-computer, pre-satellite era, without time series analyses for a comparison of time-macroscopic cycles in the biosphere with those of sunspots. Spectral components in solar wind speed or solar flares were only subsequently found in data collected by satellite. Chijevskiy deserves credit for starting a heliobiology that he regarded as an about (~) 11-year (circaundecennian) echo of the sun in the biosphere, i.e., in the treasure trove of data he accumulated and displayed graphically. The ~11-year echo turned out to be a very broad spectrum of cycles in the meta-analysis of Chijevskiy's data. Against this positive background -- qualified only by the yield of time series analyses by computer and results from satellites, as yet unavailable to him and by the recognition of the partly built-in nature of cycles -- we turn to methods, which report, in a separate abstract, the finding in Siberia of a trans- (= beyond, i.e., longer than a) year.

To be analyzed in space, near us most cells need microscopy, or far from us most stars telescopy. In time, any cycles that can be recognized as the fundamental units in and around us, near and far, also need tools for their resolution. Often, we cannot rely on a cycle's definition by the naked eye even if we can see it clearly. Very often in data with multiple cycles, some of them may not be identified. The biosphere and physics both teach us that in space and in time, cycles are often Aeolian. They may not only be missed by the unaided eye, they may not even be found by the best available methods in data covering a single cycle and/or stemming from a single geographic site.

Terms like *quasi-periodicity* and *quasi-periodic* were used by the pioneer of statistical geomagnetism Julius Bartels, the mathematician turned into a most prominent geophysicist. Bartels accounted for non-stationarities in time but not for differences as a function of space. In space as well as in time, we must realize that cycles may reveal a wind-like appearance, undergoing changes in intensity to the point of storms at one extreme and disappearance of well-established cycles at the other extreme. To reinforce the analogy of the behavior of many cycles to that of the winds, reference can be made to the latter's mythical ruler, Aeolus, to describe the spectral «non-stationarity» of novel nonphotic cycles in geographic space as well as in time.

Incidentally, Bartels regarded William Gilbert's (physician to Queen Elizabeth I and King James I of England) 1600 book as the first scientific treatise, a point in keeping with the view that science is transdisciplinary and gains from the interdisciplinary validation of ubiquitous phenomena. Bartels kindly taught his methods and described his findings to the biomedical community, i.a., in Basel, Switzerland, in 1953. At that time, when Bartels used a 24-hour period (τ) a priori for his harmonic dial, one of us (FH) reported to him that an adrenal cortical cycle can desynchronize from 24 hours, i.e., that a periodogram should precede the use of an anticipated τ fitted to the data. By now, a temporal microscopy by chronobiology and a temporal telescopy by chronomics are indispensable because the vast majority of cyclic affairs in us and around us are not only what Bartels rightly called quasi-persistent or quasi-periodic in time, but they can also be environmentally synchronized in time or desynchronized. Hence, in any meta-analysis, the stacking of data for an assumed τ (that Bartels demonstrated by stacking according to the month of the year, following an example set by Edward Sabine) should be preceded by a spectrum, for detecting new para-annual and para-semiannual τs, i.e., to identify all the components characterizing the data.

In an introduction to a book by Harlan True Stetson, Sir Edward Appleton wrote: «There are simple and fundamental reasons why collaborative effort is necessary in studying the influence of the sun's emanations on our own planet. First of all, the earth is round, and not flat. The result is that solar radiations do not impinge with equal effect on all regions of the earth's surface. The second reason is that the earth is constantly rotating; and, since interesting solar features may occur at any time, it is necessary to have observers at different terrestrial longitudes, in order that none of these interesting events may be missed. The third important fact is that the earth itself is a great magnet, and, because of this magnetic influence, electrified particles of solar origin are constrained to travel, not in straight lines, but along curved tracks. Sometimes the curvature of these tracks is so great that such charged particles impinge on the side of the earth's atmosphere which is further from the sun. In other words, we get solar effects at night. Moreover such effects occur with unequal intensity at different terrestrial latitudes because of the earth's magnetic qualities». The definition of *aeolian* (noun and adjective) recognizes that a cycle's overall global behavior in the long term may differ from its local dynamics in part of the record, just as there is the need to look for geographic differences that can change with time, e.g., among cis-half-years and far-transyears. These circumstances require GLOCAL (GLObal and loCAL) analyses recommended as a combination not only of glocal methods of analysis but also of concepts to be applied in space and time, in particular for history.

As Stetson also recognized, human minds have been able to actively change the crust of the earth in a major way (e.g., with the first atomic bomb). A course of hominization was formulated by Pierre Teilhard de Chardin, leading to his, Edouard le Roy's and most prominently the geophysicist Vladimir Ivanovich Vernadsky's noosphere of the creative mind. The latter visualized his sphere of the mind as being structured only in space by genetics. Vernadsky explicitly regarded the noosphere as being linear in time, in the sense of irreversible, and refers to the possibility that once a species is extinct, it is not likely to reappear.

In the context of a sphere of the mind, it seems pertinent that once populations rather than individuals are viewed, the diversity of species on the ocean floor undergoes cycles along the scale of millions of years, albeit with great uncertainties. Along a shorter scale, the emergence of exceptional poets, historians and physicians, about every 500 years, exhibit such cycles at a time when the cultures producing the outstanding individuals among Arabs, Chinese, Greco-Romans and Japanese did not communicate with each other, an observation in keeping with a contributory influence of the cosmos, as noted by Emil Pales with Miroslav Mikulecky. Chijevskiy, who reported, among others, and already documented ~11-year sunspot cycles' signatures in military and political affairs, assembled data, as noted, dealing with many aspects of the biosphere, including natality, morbidity and mortality, allowing the demonstration that we are actually more than (as he put it) an echo of the (circadecennian) sun. We are immersed in a sea of cycles with some environmental counterparts. Earth and sun, by weather and thereby in many other ways, compete with each other by effects which we most often have to detect by means other than our developed senses, by a temporal spectroscopy, by comparing, e.g., the amplitudes of the prominent seasonal changes averaging a calendar year length with the amplitudes of para-annual and para-semiannual components, with a CI (95% confidence interval) of their τ, covering neither the precise 1.0 or 0.5-year length, respectively.

A chronospectroscopy complements the spectroscopy of the chemical elements on earth, on the sun and in the stars. By the amplitudes in chronobiology and chronomics, we assess the relative contributions of different photic vs. nonphotic components, such as the photic, thermic and societal calendar year by comparison with the prominence of nonphotics cycles, longer than (trans = beyond) or shorter than (cis = on this side of) the year or the (geomagnetic) half-year. A new transdisciplinary spectrum emerges in which we can gauge our own physiology to detect chronopathology, starting by Chronobiologically-interpreted Ambulatory Blood Pressure and heart rate Monitoring (C-ABPM). As a dividend from C-ABPM for preventive cardiology, we indeed also gauge our own mind and well-being in a sphere of information about ourselves, personalized chronouspheres, while our emotions and thoughts may also contribute to a special, as yet spatially individualized, probably vast compartment of a generalized chronousphere, the major compartment of which is accumulating as the sum of the products of exceptional minds, now to be stored, preferably systematically, beyond books and museums, on the maturing Internet.

One exceptional mind, who wrote a popularizing history of astronomy and of some of its atavars, was Harlan True Stetson (1885-1964). His contributions constitute a good example of a brilliant, persuasive investigator who achieved much by the instruments he built and the records thus obtained and interpreted by his unaided eye. His legacy is nonetheless further improved by meta-analyses of the very data that his keen eye recognized as important but could not completely interpret insofar as he seems to be unaware of an ~5-month (quinmensal, or cis-half-year) component, constituting a tertiary fluctuation, complementing his discovery of what he called a «secondary fluctuation» and we now recognize as a trans (= beyond) year in counts of sunspots. The same limitation applies to all pioneers, including Chijevskiy and Vernadsky, who like Stetson worked in the pre-computer, pre-satellite era, so dramatically changed by Sputnik.

Even for what Stetson recognized as a secondary fluctuation, an analysis of its uncertainties is helpful, if one can conclude from the CIs (95% confidence intervals) computed from records of different lengths that they indeed overlap each other. Hence the phenomenon Stetson reported was consistently statistically significant as the record lengthened, albeit the aeolian point estimates of τ are not identical in the two analyses. In that context, it cannot be overemphasized that stacking, according to clock hour, day of the week or, as often in physics, biology, sociology or economics, by the month of the year, can obscure or eliminate certain rhythms that deviate in length from that which may occur along the time scale chosen for stacking. Sometimes, as in the Siberian data of one of us (DG) a transyear may represent the only real component. In data unobscured by stacking along the hours of the day or days of the calendar week, a month, a year or a decade, there are many cycles and coperiodisms that cannot be assessed without turning to the original unstacked data.

To one of us, (FH), as already noted, the finding of τs different from 24 hours in cortical adrenal function was the reason for first advocating a periodogram before assessing a predetermined τ such as that of the 24-hour day. The computation of a periodogram (now preferably of a nonlinearly extended cosinor spectrum) and eventually, we hope, yet better glocal methods should come first. Computing spectra, before analyzing yearly or half-yearly stacked data, allowed also the finding of biospheric quinmensals, reported as ~154-day τs, also first in physics. More of the τs of clinical interest in the cardiovascular system were first reported in physics, notably in astronomy and geophysics, the northern lights included, while some other τs were apparent early in economics or were first analyzed in the biosphere. Further of interest, many historically interesting cycles exist in archives awaiting analysis, in some cases with methods that were available when the data had been collected. Centuries passed before data on sunspots retrieved by Franz Daxecker from Christoph Scheiner's publications were explicitly interpreted as a circaundecennian cycle.

An about-decadal cycle is assessed, as in the case of Scheiner's data with its uncertainities and so is a transyear and a quinmensal component, in data published by Stetson half a century before the same cycles were predicted by Wolff and found by Rieger et al. or reported by Richardson et al. By the same token, meta-analyses on Egeson's data validated in the microscopic period domain the inferences drawn by him with his unaided eye. Meta-analyses validated the work by the Dыlls in the phase domain. We found a physiological record that has a CI of its transyear congruent with (overlapping the CI of) the entire record available for solar wind speed (SWS) yet does not overlap the τ of SWS during the span concurrent with the physiological record. This observation could be interpreted as an indication of the genetic coding of cycles that may be more important in their origin then the concurrent driving exerted by their cosmic counterpart, such as SWS. This finding supports the critical results in the biosphere of the removal and/or replacement of an environmental spectral component. The best remembrance of Gennady Gubin is by the findings with respect to the ontogeny of the cardiovascular system: a histogram of the τs in decade-long data from 8 individuals, there is a peak at about 10 years. Metaanalyses of all of the τs found in data collected by Chijevskiy, Douglas, Wheeler, and, among others, by ourselves, show a peak of τs at ~20 years in a histogram and are yet more persuasive of an effect in the biosphere of the cosmos, past and/or present. While the peaks in a histogram can be used as hint of current partial driving by the cosmos, the cycles with τs other than those at peaks, point to other decadal cycles that may be free-running. In an individual, there can be a peak at a harmonic of a decadal cycle, at ~5 years, in a set of 14 variables studied during wakefulness for ~45 years. Most interestingly, a global analysis shows that mentality can have only a transyear. Indeed there are many τs found in individuals and populations at a τ longer than 1 year, a new landscape of novel biospheric cycles.

We are glad to see Siberian contributions to the comparison of seasonality with para-seasonality, and thereby an assessment of the effect of our cosmos competing with the photic, thermic and societal seasons, with nonphotics winning in the circulation of Siberians and Minnesotans.

BIOSPHERIC-TERRESTRIAL COPERIODISMS, A TRANSYEAR AND A QUINMENSAL FROM A META-ANALYSIS

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A brief entry on Harlan True Stetson (1885-1964), an American astronomer and physicist, succinctly describes his education:

«He earned a B.S. from Brown University in 1912, a M.A. from Dartmouth College, then a Ph.D. at Harvard University in 1915. His thesis was titled, *On an Apparatus and Method for Thermo-Electric Measurements for Photographic Photometry*.

«Stetson joined Dartmouth in 1918 to teach physics, and then moved to Harvard where he taught astronomy until 1929. He then became the director of the Perkins Observatory.

«In 1936 he joined the Massachusetts Institute of Technology. He directed the MIT Cosmic Terrestrial Research Laboratory from 1940 until 1950, and performed research into the relationship between the cosmos and the Earth. His studies included sunspots, the Earth's crust, and the propagation of radio waves.

«The crater Stetson on the moon is named after him.»

Five publications are then listed (1-5).

Here we complement information about him: Stetson constructed instrumentation to automatically record radio intensities at the Perkins Laboratory at Harvard. In so doing, he discovered that radio waves and counts of sunspot numbers followed an opposite time course in a (typical) 2-month record in order to display a largely similar time course apparent to the naked eye. He then inverted the curve of sunspot numbers and plotted it along with the strength of the radio signals he measured. Next, he discussed during 1922-1929 a 15-month (1.26 year) «secondary fluctuation» which upon meta-analysis covers, with the CI (95% confidence interval) of its period (τ) the 1.33-year periodicity discovered from MIT in solar wind speed over 50 years later (6; cf. 7, 8) for which there are signatures in the biosphere (9-20) in human natality, called Halberg's transyears (11) and Halberg's para-seasonality (17).

Our meta-analyses of Stetson's data reveal the about-154-day period, called quinmensal or cis-half-year, corresponding to a prediction by Charles Wolff in 1983 (21), found in 1981 by Rieger et al. (22), amply confirmed in physics (23-60) as in the biosphere (9-20; cf. 61, 62). All of these meta-analyses could have been carried out in 1937 with methods available since 1801 (63). This detracts neither from Stetson as a rigorous, albeit time-macroscopic, scientist who recognized effects of the sun with hard data and found cycles later confirmed in physics that are strongly reflected in the human cardiovascular system, nor does it detract from Stetson who was also, secondarily not primarily, an extraordinarily fine popularizer of science who paid tribute in turn to his atavars.

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WRIST ACTIVITY: MARKER OF INFRADIAN MAGNETIC CYCLES?

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Human wrist activity could be a lifetime unobtrusive marker as such (1) and eventually as part of a multi-variable recorder or Polychronor (2). It was recorded for about 21 months, with interruptions, by two women (OS, starting at 89 years of age, and GC, starting at 61 years of age) and one man (FH, 92 years of age at start of study) (1). Sampling was at 32 Hz with an instrument from Respironics, with integrated counts recorded at 1-minute intervals. Data were averaged over consecutive 5-minute intervals prior to analysis by the linear-nonlinear cosinor and chronobiologic serial sections (3-5). An anticipated about 5-month (quinmensal) component was detected in the actigraphy of 3 subjects (Table 1). Shorter than 6 months, it is called a cis-half-year (cis = on the near side of 6 months). In geophysics, a cis-half-year had been predicted by Charles Wolff (6) and found in solar flares by Rieger et al. (7), later confirmed by many physicists. A cis-half-year had also been found by our meta-analyses of sunspot counts published by Stetson in 1930 (8; cf. 1).

The cis-half-year in actigraphy was found by serially dependent sampling as to individuals, in keeping with an earlier serially dependent demonstration of this component in longitudinal records of heart rate and blood pressure of a clinically healthy man (9) and in longitudinal data series of urine volume and the urinary excretion of 17-ketosteroids from another clinically healthy man (10). A cis-half-year was also documented by transverse sampling on a population basis in circulating melatonin of patients, each individual studied at 4-hourly intervals for only 24 hours (11).

As compared to the much larger amplitude of the circadian component, the amplitude of the cis-half-year in actigraphy is relatively small (Table 1), yet it is a definitive peak in the spectrum. A secondary peak at a period of about 0.33 year also characterizes FH's systolic blood pressure, monitored automatically around the clock at 30-minute intervals

Table 1

About 5-month cycles (quinmensals)* in human motor (wrist) activity

Period (years, y; days, d; or hours, h) [CI]	Amplitude (count***) [CI]	(% of 24-h amplitude)
OS (F, 89 y of age at start of study)		
0.7728 y [0.6675, 0.8781]	0.459 [0.145, 0.773]	(9.50)
0.4160 y [0.3664, 0.4655]	**0.305 [0.024, 0.585]**	**(6.31)**
0.2324 y [0.2125, 0.2522]	0.252 [-0.01, 0.515]	(5.22)
24.00 h	4.83 [4.58, 5.09]	–
GC (F, 61 y of age at start of study)		
0.4100 y [0.3920, 0.4279]	**0.555 [0.389, 0.721]**	**(9.07)**
24.00 h	6.12 [5.95, 6.29]	–
FH (M, 92 y of age at start of study)		
1.860 y [1.527, 2.193]	0.990 [0.806, 1.170]	(18.00)
0.4536 y [0.4179, 0.4892]	**0.481 [0.275, 0.687]**	**(8.75)**
0.3367 y [0.3237, 0.3496]	0.699 [0.493, 0.905]	(12.71)
24.00 h	5.50 [5.30, 5.70]	–

*Originally also referred to as cis-half-years (cis = on the near side, i.e., shorter than).
**CIs: 95% confidence intervals.
***Count from digital integration with a unit from Respironics.

during 26 years (with interruptions). It is occasionally found in biospheric time series instead of the cis-half-year or in addition to it. A cis-half-year was not detected in the activity data of JF, a woman with a 22-year history of twice-yearly adynamic depression and circadian behavioral desynchronization during depressive episodes. During such times, synchronization to a double tidal period of about 24.8 hours was apparent in JF's wrist activity, as well as in several other variables measured concomitantly, albeit with a lesser sampling rate (12). Multiple circadian periods competing with each other were isolated in several variables thereafter (13). As for circadian desynchronization, serial sections demonstrate it most clearly in automatically recorded vascular variables by a chronobiologically-interpreted ABPM (C-ABPM).

Whereas a cis-half-year was not detected in the activity data of JF, there is a possible frequency multiplication to a component of about 73 days. Similar periods are, of course, no proof of causal relations. Long-term monitoring of wrist activity by more than three clinically healthy subjects is necessary before the use of wrist activity can be considered to assess infradian variability in the biosphere. Results from the available records thus far suggest possible differences in the cis-half-year period of wrist activity of different subjects, its point estimates for OS and GC lying outside the 95% confidence interval of FH's period (Table 1). Longer records are needed before clear differences can be documented, as the 95% confidence intervals of the 3 subjects overlap. The spread of cis-half-year periods found thus far in biology exceeds that listed in Table 1, while the dispersion of global point estimates of the «154-day» periods reported from the physical environment is relatively small. Time-varying analyses reveal marked changes in the cis-half-year period in physical variables and in their biological counterparts. In physics, the variability is such that one of the now-prominent mentees of an outstanding mentor, who published pertinent observations, actually doubted their reality in subsequent correspondence (personal communication by Yosuke Kamide). The even greater biospheric variability of cis-half-years and other para-semiannual and para-annual oscillations prompted a meeting of physicists and biomedical scientists to name them «aeolian» (14). These aeolians are of medical interest: they characterize human cardiac arrhythmia and sudden cardiac death (15, 16).

By contrast to cis-half-years, in 6 residents of a home for assisted living in Finland, 3 of them had half-yearly components in their telemetered activity. It must be noted that the 6 subjects in Finland needed help in daily activities but the Minnesotans did not. With this qualification, 3 of the Fins carried signatures of geomagnetism (the half-year component) while the 3 Minnesotans had a heliomagnetic (quinmensal) signature. Important is the added finding that in all 9 subjects there was no demonstrable circannual component. In the human elderly, whether or not on assisted living, effects of the seasons, if any, may be overcome by other factors, including helio- and/or geo-magnetism.

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WHEN TO EAT AS WELL AS WHEN TO TREAT

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Minnesotan work on meal timing in mice, catfish and humans has been reviewed (1-4). Timing access to food for singly housed mice in cool temperature can make the difference between survival and death (5). In humans, the timing of a meal in relation to awakening, in studies involving a single daily meal, consumed as Breafast only (B), within 1 hour after awakening, versus Dinner only (D), consumed 12 hours after awakening, was studied with fixed calories per meal and limited activity first and thereafter with the free choice from an assortment of foods. Meal timing in these studies was more important than meal size in determining outcomes with respect to relative body weight change. This result is in keeping with a differential shift in circadian acrophase by meal timing of different endocrine and other variables: the circadian rhythm in cortisol was shifted but little by the change from B to D or vice versa. By contrast, the circadian rhythms of insulin and glucagon were greatly displaced depending on whether the single daily meal was breakfast or dinner. The biochemical environment within the body is drastically different on different meal times.

The studies on free choice meals and on those involving a fixed number of calories both showed, on the average, a relative body weight loss on B as compared to D, even though subjects in the fixed calorie study ate the identical number of calories (2000 Kcal) prepared by two dieticians every other day, whereas in the free choice study, they consumed a daily average of 1713 Kcal on B and 2139 Kcal on D. This difference in weight loss was significant ($p<0.05$) and is contrary to what would be anticipated without a consideration of timing. Even though subjects consumed fewer calories at breakfast in the free choice meals than in the fixed calorie meals, the relative weight loss was less in the former than in the latter study ($p<0.05$).

Other chronobiologic aspects relating to nutrition include the finding of Vascular Variablity Anomalies (VVAs) that signal a pre-metabolic syndrome (6, 7). Just as we advocate personalizing our dealing with blood pressure (rather than using diagnostic targets) by Chronobiologically-interpreted Ambulatory Blood Pressure Monitoring (C-ABPM) (8, 9), and suggest individualizing treatment timing to do no harm yet help (10), the timing of physical activity can also be optimized for the given individual (11, 12), as it can for any intervention, including nutrition, as the choice of meal times can override the effect of meal size (1-4).

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SLIDING LENGTHENING SPECTROGRAMS ASSESS FAMILIAL ADULT-TO-ELDERLY HUMAN AGING IN THE BLOOD CIRCULATION

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As our concomitantly recorded biospheric as well as environmental time series lengthens, we can take a more comprehensive look at how we interact with habitats, near and far. Temporally global summaries, such as spectra analyzing a time series as a whole, can be complemented by a temporally local examination of the behavior either of a given period (τ) or of a broader spectral region. Thus, we find out whether and, if so, how one or several neighboring τs change as a function of time and/or series length. Analyses are usually carried out linearly in the reciprocal of τ, the frequency (f). Chronobiologic serial sections, as part of a microscopy in time of happenings in ourselves, or in our affairs, focus on a given selected biologic τ's characteristics, varying, i.a., with age or following an intervention. Chronomic serial sections, as a telescopy in time, aligning environmental data with τs corresponding to biologic ones, can examine the extent of an (auto- and/or induced) resonance of a biospheric cycle with a given concomitantly recorded external time series.

Herein, we introduce a temporally local method, a sliding spectrogram, consisting of windows of systematically increasing length (slides). These complement gliding spectrograms, i.e., spectra of consecutive sections of a time series of fixed length, displaced by a fixed increment in a local gliding spectrum. The gliding spectrum has been aligned, along the same ordinate of τ, with an added spectrum of the entire time series, in order to render it temporally global as well as local, i.e., glocal. Such glocograms, as compared to conventional wavelets, have the merit of providing numerical point and interval estimates such as CIs (95% confidence intervals) of both the τ and of the corresponding amplitudes (As) for each globally prominent τ.

The complementary sliding spectrogram approach was applied, after interpolation, to serial self-measurements by a father (SBS), his wife (SIS) and their son (RBS). The parents self-measured blood pressure and heart rate for nearly 3 or 2 decades, respectively, every day, in the morning and in the evening, with few interruptions. Their son self-measured or self-rated 14 variables about (~) 6 times during each wakefulness span for ~45.65 years. This methodologic illustration of lengthening sliding windows describes, on a single family basis, para-annual changes during aging. In RBS, who started self-surveillance in his 20s, there is a change in his blood circulation from calendar year dominance, in most of the first 4 decades of adult life, in some but not all variables, to transyear dominance (in RBS's late fifties), seen more clearly globally in his parents. In RBS it can also be seen that a mental function, his 1-minute estimation, exhibits only transyears globally, although in some short intervals, temporally locally, there is great variability in the para-annual spectra region. Added spectra of all 3 subjects' entire time series render the overall approach glocal (global & local in time), awaiting complementary glocality in space, by others who follow the example set by the RBS family in other geographic locations.

As a whole, our analyses are in keeping with the assumptions that 1. spectral lines found globally, when examined over long spans of over 4.5 decades in sliding spectra are locally bands rather than lines, representing aeolian behavior. 2. Spectral components with a longer than a calendar year, viewed either (locally) as broad bands or (globally) as narrower bands corresponding to spectral peaks, the latter with a CI of their not overlapping 1.00 year, can coexist with a 1.00-year component (e.g., in blood pressure) or can occur in the absence of a consistent precise 1-year component (e.g., in the estimation of 1 minute) in the same person; 3. with advancing age, overall transyear prominence can overshadow that of the calendar year, when expressed as a ratio of As, namely A(transyear)/A(calendar year). This occurs in variables wherein a calendar year was dominant during adulthood up to and including the early fifties; 4. transyears represent a distinct transdisciplinary (bio- as well as abiospheric) entity of both space and earth magnetism and of the (magnetism of the) human body, separate from an about yearly (circannual) rhythm; 5. A local and, in particular, a global analysis of environmental and biospheric data both allow the separation of near- and far-transyears, globally with non-overlapping CIs, also validated by sliding as well as gliding spectrograms locally.

We postulate, on the basis of these and other meta-analyses that the relative importance of the photic, thermic and societal seasons vs. nonphotic factors involved in human physical and mental health and disease and other economic, military and political affairs can be gauged by the relative prominence of different components in a transdisciplinary spectrum of cycles in order to explore biotic-abiotic associations. In the latter context, it seems critical that in RBS's parents and in other elderly men (FH and GSK), systolic blood pressure showed only a transyear and no calendar year component and that in one of them this transyear of 1.3 years was dampened, its band narrowed, yet it persisted when the solar wind speed (SWS) did not allow the demonstration of this component. The about 1.3-year spectral component also persists in terrorism in two of 3 populations, when its coperiodism in SWS was not detected. As an aside, in a set of over 600 C-ABPM records' diastolic blood pressure, transyears again dominate.

DIFFERENT CYCLES CAN MODULATE IMPUTED CARDIOVASCULAR SERIES OF CIRCADIAN CHARACTERISTICS VS. ORIGINAL DATA'S CYCLES

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Obviously different periodicities characterize phenomena as varied as the heart and respiratory rates, sleep and wakefulness, and menstruation. There are also different multiple periodicities in different, e.g., nervous vs. cardiovascular, organ systems and within each of these systems. Even in one and the same variable, such as the urinary excretion of steroidal breakdown or other products (1), there are circadian and about (~) decadal periodic intermodulations, with, among others, an about 7-day rhythm and with what originally appeared to be a desynchronized circannual rhythm, yet was eventually identified as a set of para-annual components and a para-semiannual component (2). Here we demonstrate, for each in a set of variables from the cardiovascular system of an elderly man, GSK, receiving hypotensive treatment (3), who surveyed himself by Chronobiologically-interpreted automatic Ambulatory Blood Pressure Monitoring (C-ABPM) at 30-minute intervals for ~14.7 years, that different periods, τ, in keeping with non overlapping CIs (95% confidence interval) of τs, can be found in original data of his blood circulation on the one hand and in new series isolated by imputation (intermediate cosinor computation) on the other hand: the τs in 3 new series are derived from the original data by cosinor, i.e., the τs from separate daily series of MESORs, M, versus daily 24-h amplitudes, A, and daily 24-hour acrophases, ϕ, can differ among them and from those in original data.

Some different τs can be anticipated from the fact that the sample size (and perhaps noise) has been reduced by the intermediate cosinor computation (imputation), in particular when comparing 24-h Ms with the series from which the M is derived. The A and ϕ, as gauges of the extent versus the timing of the daily changes, are more likely coordinated by mechanisms that are partly different for A vs. ϕ and differ from those underlying the M, since they already underlie different diagnoses. It seems likely that some factors for temporal coordination may affect all aspects of a given variable. Therefore, one expects to (and does) find, in the imputed series, many τs with overlapping CIs, while in the case of partly different mechanisms, τs with non-overlapping CIs are anticipated (and found). This is indeed the case for all variables summarized for GSK and for others whose data are thus far analyzed both as original data vs. Ms, As or ϕs of systolic and diastolic blood pressure, pulse pressure, heart rate and the systolic blood pressure x pulse product (2).

Different aspects of the dynamics of the variables investigated in the circulation of blood undergo varied cycles of basic and applied interest, the mechanisms of which remain to be established now that their occurrence is documented systematically for the original data as well as in 24-h Ms, 24-h As and 24-h ϕs for all variables derived from C-ABPM, all of diagnostic interest: they underlie cardiovascular disease risk assessment and can lead to the diagnosis of vascular variability anomalies, VVAs, which, when coexisting, changed the risk of an ischemic brain attack within 6 years in one study from less than 10 to 100% (4). VVAs constituted sensitive gauges of high cardiovascular disease risk in other studies as well (5; cf. 6-9).

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