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Rules of Heliogeomagnetics Diversely Coordinating Biological Rhythms and Promoting Human Health

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Featured Application: Resolving the complexity of heliogiomagnetic effects on human physiology by considering several rules, including their bell-shaped dose-responses for health maintenance, should contemplate "chronobioethics", a resonance of biological rhythms, brain plasticity, and psychological resilience.

Abstract: This investigation reviews how geomagnetic activity affects the circadian variation in blood pressure (BP) and heart rate (HR) and their variabilities of clinically healthy individuals. A small study in Alta, Norway (latitude of 70.0° N), serves to illustrate the methodology used to outline rules of procedure in exploring heliogeomagnetic effects on human physiology. Volunteers in the Alta study were monitored for at least 2 days between 18 March 2002 and 9 January 2005. Estimates of the circadian characteristics of BP and HR by cosinor and the Maximum Entropy Method (MEM) indicate an increase in the circadian amplitude of systolic (S) BP on geomagnetic-disturbance days compared to quiet days ($p = 0.0236$). Geomagnetic stimulation was found to be circadian-phase dependent, with stimulation in the evening inducing a 49.2% increase in the circadian amplitude of SBP ($p = 0.0003$), not observed in relation to stimulation in the morning. In two participants monitored for 7 days, the circadian amplitude of SBP decreased by 23.4% on an extremely disturbed day but increased by 50.3% on moderately disturbed days ($p = 0.0044$), suggesting a biphasic (hormetic) reaction of the circadian SBP rhythm to geomagnetics. These results indicate a possible role of geomagnetic fluctuations in modulating the circadian system.

Keywords: ambulatory blood-pressure monitoring; cardiovascular circadian rhythm; circadian amplitude; circadian acrophase; circasemidian (about 12 h) rhythm; bell-shaped dose-response; weaker or stronger intensity of geomagnetic stimuli; circadian-phase-dependent response; subarctic area

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1. Introduction

The discovery of the circadian rhythm and the finding that the circadian clock coordinates half the mammalian protein-coding genome indicate the importance of time considerations for human health and life more generally [1–6]. Studies on genetic animal models and on humans provide evidence that circadian disruption associates with metabolic and psychiatric disorders, cancer, cardiovascular diseases, and cognitive decline in the elderly [7–17].

Our previous investigations [18–20] suggested that magnetic fluctuations in space conveyed a possible anti-aging effect: The power of the HF-component of heart rate variability (HRV) increased and the nocturnal dip in HR became more pronounced on days with higher versus lower magnetic activity. The circadian HR rhythm was also amplified by the circasemidian (about 12 h) component of geomagnetic fluctuations. Moreover, the circadian amplitude of the VLF-component of HRV was highly correlated with the 24 h, 12 h, and 48 h amplitudes of the geomagnetic declination index. The VLF-component is clinically important since it is an indicator of health and well-being. Reduced values are predictive of morbidity and mortality from cardiovascular disease [18–26]. Since physiological processes critical for life fluctuate with different frequencies, many of them shared with the near and far environment [27–29], it is no surprise that periodic components of space weather are associated with an amplified circadian HR rhythm in space. Non-photic fluctuating cosmic factors (such as magnetic disturbances and solar activity) can affect virtually every cell and electrical circuits in biological systems [30–32]. Since space weather affects humans, Halberg et al. [33] proposed that chronomes (i.e., broad time structures) in biota (including humans) resonate with environmental cycles. Their study is part of chronoastrobiology. For instance, on Earth, about 7-day (circaseptan) rhythms in human HR were more prominent during spans when they were detected in solar activity than when they were not [31].

Possible health hazards of natural, solar-variability-driven temporal variations in the Earth's magnetic field have been controversial due to inconsistent results over the past half century. Researchers evaluated how the physical environment, including variables such as the natural variation in the geomagnetic field in and around the Earth, affect biological processes [34–50] and human health [28,51–63]. Studies were conducted in the laboratory and in the field. Environmental–organismic interactions were investigated in citizens living in magneto-biotropic regions, including subarctic and arctic areas [64].

Herein, we illustrate the methodology used to assess effects of space weather on human physiology by analyzing data from ambulatory blood-pressure monitoring (ABPM) obtained from clinically healthy citizens in Alta, Norway. Specifically, we examine whether changes in geomagnetics affect their BP variability, focusing on circadian characteristics. Results are interpreted within the larger context of our previous studies of heart rate variability in Alta as well as on the International Space Station (ISS), leading to the proposition of rules of procedure in exploring heliogeomagnetic effects on human physiology.

2. Materials and Methods

2.1. Subjects

Overall, 36 citizens of Alta, Norway, agreed to perform 7-day/24 h ambulatory BP monitoring (ABPM), but 20 were excluded according to the following criteria: missing data due to the interruption or suspension of monitoring (n = 8); monitoring lasting less than 48 h, preventing the reliable assessment of circadian characteristics (n = 7); taking medicines for diseases (n = 5), including hypertension (n = 2), hypothyroidism (n = 2), or peri-menopausal syndrome (n = 1). The remaining 16 participants (8 men, 20 to 55 years of age, mean ± SD: 40.1 ± 7.9) were eligible for inclusion in this study, Figure 1. They were confirmed to be normotensive by conventional [65,66] and chronobiological [67–69] guidelines. Between 18 March 2002 and 9 January 2005, 5 performed ABPM for over 5 days and 11 for over 2 days.

2.2. Ambulatory BP Monitoring

Non-invasive ABPM was carried out using an oscillometric monitor (TM-2431, A&D, Tokyo, Japan) to measure systolic SBP, diastolic (D) BP, and HR. The monitor was programmed to use a sampling interval of 30 min between 07:00 and 22:00 h and 60 min between 22:00 and 07:00 h for 7 days. Study participants were fitted with the monitor at the town office and returned to the office 7 days later. They were instructed on how to use the monitor and to remove it while taking a bath. They were asked to record the times they went to sleep and woke up.

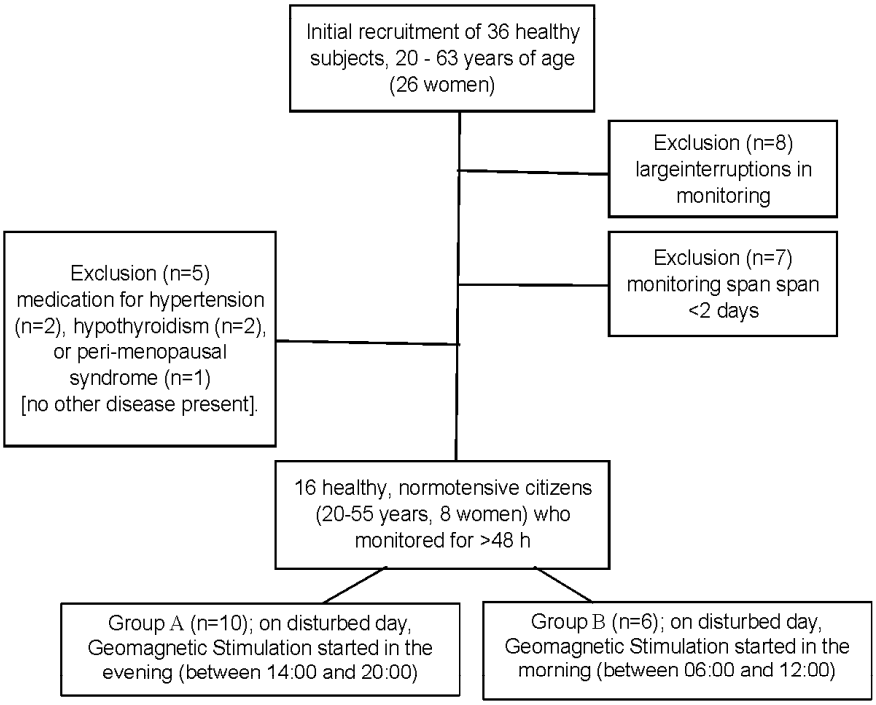

Figure 1. Consort flowchart.

2.3. Geomagnetic Monitoring

A geomagnetic record was obtained at 1 min intervals from the Auroral Observatory of the University of Tromsø, in Tromsø, Norway (latitude 69°39′ N, longitude 18°56′ E). The following variables were considered: declination (D), angle between geographic and magnetic north (°); horizontal intensity, H (nT); vertical intensity, Z (nT); inclination (Inc); angle between horizontal plane and magnetic direction (°); and total field intensity, F (nT).

In records spanning 2 days, the quiet and disturbed days were defined as those 24 h days with the lowest or highest geomagnetic activity. This definition is the same as that used in our previous studies of HRV in Alta and in space [18,70–72]. In the two records spanning 5 days or longer, moderate and extreme geomagnetic disturbances correspond to geomagnetic activity 3 or 12 times higher than on quiet days, respectively.

2.4. Circadian Parameters of BP and HR

Each record was analyzed by MEM (MemCalc/Win, Suwa Trust GMS, Tokyo, Japan) [73] to estimate the circadian period of SBP, DBP, and HR. The period was determined to be the inverse of the frequency corresponding to a peak in the MEM spectrum located in the vicinity of 1/24 (h^{-1}). Missing data were linearly interpolated prior to analysis.

A single cosine curve with a period of 24 h (or other fixed period when indicated) was fitted independently to the same data by cosinor [69,74,75] to estimate the amplitude and acrophase (phase of the maximum in relation to local midnight, used as reference time) in addition to the MESOR (Midline Estimating Statistic Of Rhythm, a rhythm-adjusted mean). This model was applied to subspans of each record, determined based on the geomagnetic indices at the time of monitoring. Changes in circadian parameters (MESOR, amplitude, and acrophase) between different subspans assessed their response to geomagnetic activity.

2.5. Data Analysis

Data were expressed as mean ± standard deviation (SD). Effects of magnetic activity on circadian profiles of BP and HR were assessed by computing differences between their values assumed during geomagnetically quiet and disturbed conditions, analyzed by the paired *t*-Test. *p*-values less than 0.05 were considered to indicate statistical significance.

3. Results

3.1. Changes of Biological Characteristics of BP and HR Associated with Geomagnetic Disturbances

First, the effect of geomagnetic disturbances on BP and HR variabilities of all 16 participants is examined on the basis of 2-day ABPM records including geomagnetically quiet and disturbed days. Table 1 (top) summarizes changes in circadian and circasemidian parameters of BP and HR related to geomagnetic activity. The circadian amplitude of SBP increased by 29.7% (from 13.8 to 17.9 mm Hg; $p = 0.0236$), while the circasemidian amplitude decreased by 27.6% (from 10.5 to 7.6 mm Hg; $p = 0.0529$). The circadian acrophase of SBP and DBP was delayed on disturbed days compared to quiet days (SBP: from 15:08 to 16:14, $p = 0.0574$; DBP: from 15:05 to 16:55, $p = 0.0463$), whereas the circasemidian acrophase did not change statistically significantly. No change in SBP or DBP MESOR was found between geomagnetically disturbed and quiet days.

Table 1. Changes in heart-rate and blood-pressure characteristics along with geomagnetic activity observed in the 24 h span.

	State of Geomagnetic Activity	**Quiet (n = 16)**		**Disturbed (n = 16)**		**Paired *t*-Test**	
	Variable (Units)	**Mean**	**SD**	**Mean**	**SD**	**t-Value**	***p*-Value**
Circadian Characteristics of BP and HR	SBP-M (mmHg)	119.8	9.7425	119.8	11.8	0.023	0.982
	SBP-A(24 h) (mmHg)	13.8	4.3158	17.9 (129.1%)	5.8	2.52	0.024
	SBP-ϕ(24 h) (hour:min)	15:08	1:37	16:14	2:11	2.058	0.057
	DBP-M (mmHg)	74.1	6.8	72.1	6.1	−1.745	0.102
	DBP-A(24 h) (mmHg)	11.3	4.8	10.6	5.9	−0.38	0.709
	DBP-ϕ(24 h) (hour:min)	15:05	1:56	16:55	3:54	2.172	0.046
	HR-M (bpm)	67.2	7.1	68.2	7.4	1.035	0.317
	HR-A(24 h) (bpm)	8.3	3.8	9.7	3.4	1.567	0.138
	HR-ϕ(24 h) (hour:min)	14:17	2:33	14:46	3:57	0.471	0.644
Circasemidian Characteristics of BP and HR	SBP-M (mmHg)	118.4	9.7	119.8	11.7	0.827	0.421
	SBP-A(12 h) (mmHg)	10.5	2.9	7.6 (72.4%)	4.7	−2.101	0.053
	SBP-ϕ(12 h) (hour:min)	19:08	6:36	17:51	5:02	−0.815	0.428
	DBP-M (mmHg)	73.3	6.8	72.7	6.6	−0.478	0.640
	DBP-A(12 h) (mmHg)	9.0	4.2	6.0 (66.7%)	4.3	−2.029	0.061
	DBP-ϕ(12 h) (hour:min)	19:18	6:38	16:30	5:52	−1.428	0.174
	HR-M (bpm)	67.1	7.0	67.9	7.3	0.827	0.421
	HR-A(12 h) (bpm)	5.0	3.1	4.2	2.6	−0.7	0.495
	HR-ϕ(12 h) (hour:min)	12:57	7:58	16:03	5:34	1.412	0.179
Circadian Characteristics of Geomagnetics	M: Declination (degree)	3.65	0.19	3.69 (101.0%)	0.2	3.564	0.003
	A(24 h): Declination (degree)	0.09	0.05	0.18 (207.0%)	0.1	4.499	0.0004
	ϕ(24 h): Declination (hour:min)	2:01	1:55	1:54	1:47	−0.328	0.747
	M: Horizontal component (nT)	11,020.5	26.0252	10,997.3 (99.8%)	39.9	−2.499	0.025
	A(24 h): Horizontal component (nT)	52.3	61.58	108.4 (207.4%)	75.0	3.754	0.002
	ϕ(24 h): Horizontal component (hour:min)	15:13	4:23	13:06	3:08	−3.027	0.009
	M: Vertical component (nT)	51,980.8	39.8312	51,984.6	46.4	0.965	0.35
	A(24 h): Vertical component (nT)	17.1	15.1	33.8 (197.6%)	23.0	3.994	0.001
	ϕ(24 h): Vertical component (hour:min)	12:44	6:26	18:49	7:44	3.227	0.006
	M: Inclination (degree)	78.03	0.03	78.06 (100.03%)	0.1	2.5	0.025
	A(24 h): Inclination (degree)	0.05	0.07	0.12 (223.3%)	0.1	3.856	0.002
	ϕ(24 h): Inclination (hour:min)	12:20	9:44	10:08	10:13	−2.957	0.001
	M: Total field intensity (nT)	53,136.2	36.8631	53,135.4	42.1	−0.241	0.813
	A(24 h): Total field intensity (nT)	20.3	15.6	26.2	13.1	1.191	0.252
	ϕ(24 h): Total field intensity (hour:min)	14:57	3:38	17:47	6:48	1.71	0.108

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; M: MESOR; A: Amplitude; ϕ: Acrophase; Data analyzed over 24-h spans.

Second, Table 1 (bottom) compares geomagnetic characteristics between the quieter and more disturbed day of each of the individual 48 h records. The MESOR of D (declination), Inc (inclination), and H (horizontal component) were statistically significantly higher on the more disturbed than on the quieter days. The circadian amplitude of these geomagnetic variables and of the vertical component (Z) were about twice as large on disturbed compared to quiet days. The circadian acrophase of H and Inc were significantly advanced by about 2 h on disturbed days, while the circadian acrophase of V was delayed by about 6 h compared to quiet days.

Next, we show the involvement of geomagnetic activity on the circadian rhythm of BP by regressing the circadian characteristics of SBP on disturbed days as a function of the MESOR of geomagnetic indices. D showed the strongest association, as illustrated in Figure 2, suggesting that magnetic fluctuations may modulate the circadian rhythm of SBP.

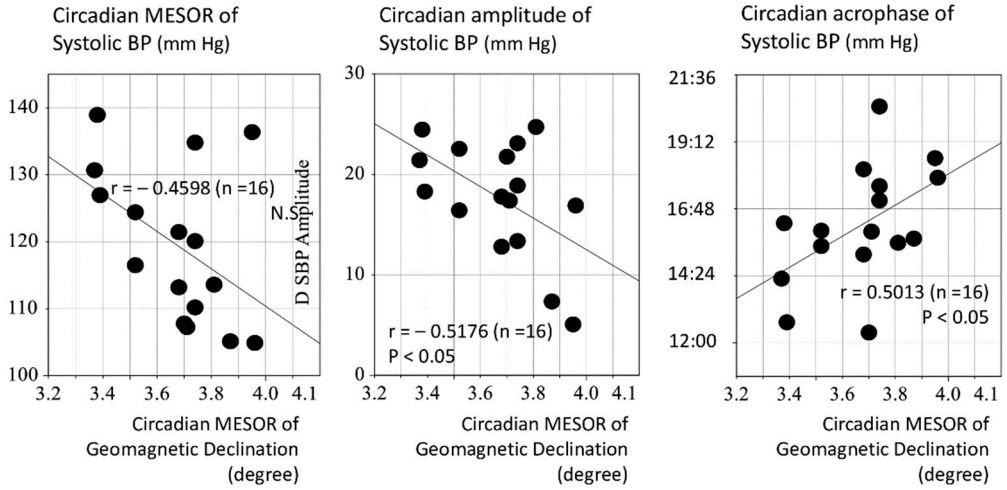

Figure 2. Effects of magnetic fluctuations on the circadian parameters of SBP on geomagnetically moderately disturbed days. Circadian MESOR and amplitude of SBP on disturbed days correlate negatively with statistical significance with the circadian MESOR of geomagnetic declination (left and middle, respectively), while the circadian acrophase of SBP is delayed (right). These results suggest that the circadian parameters of systolic BP are affected by magnetic fluctuations on moderately disturbed days, i.e., about 3 times higher on moderately disturbed days compared to quiet days.

3.2. Assessment of the Effect of Magnetic Fluctuations on the Circadian Period

To verify any involvement of geomagnetic fluctuations on the circadian period, in ABPM records spanning more than 5 days, two continuous 24 h spans were identified to correspond to quiet geomagnetic conditions and two other 24 h spans when geomagnetic conditions were disturbed. No difference in circadian period was found between quiet and disturbed conditions in the 5 participants monitored for more than 5 days, Table 2 (top).

As a response to geomagnetic disturbances, both SBP and HR showed a statistically significant increase in circadian amplitude, compared to geomagnetic quiet conditions, Table 2. The circadian amplitude of SBP increased by 68.5% (18.8 vs. 11.1 mmHg, $p = 0.0016$) and that of HR by 23.8% (9.4 vs. 7.6 bpm, $p = 0.0224$). The MESOR and circadian acrophase of these variables were not affected.

Slight differences in results from these 5 participants (Table 2) compared to those from all 16 volunteers (Table 1) may stem in part from larger differences in geomagnetic conditions in the former than in the latter case, as shown in the lower part of Table 2. Then, on disturbed days, in the absence of differences in MESOR, the circadian amplitude of geomagnetic indices increased about 2.5 times (1.5 to 3.0) compared to quiet days. D increased about 2.5 times from 0.095° to 0.231° ($p = 0.0076$), Z about 3.0 times from 8.19 to 25.35 nT ($p = 0.0157$), and F about 1.5 times from 15.32 to 24.13 nT ($p = 0.0247$).

Table 2. Circadian characteristics of blood pressure (BP) and heart rate (HR) on days of moderate geomagnetic disturbances versus quiet days *.

Variable (Circadian Parameter)		Two 48-h Spans of BP and HR				
		Quiet Days (n = 5)		Disturbed Days (n = 5)		Paired *t*-Test
		Mean	SD	Mean	SD	*p*-Value
SBP (mmHg)	τ	23.4	1.5	24.122	2.0	0.584
	M	122.1	12.2	121.7	13.1	0.929
	A	11.1	3.3	18.8 (168.5%)	3.3	0.002
	ϕ	15:10	1:16	15:37	1:53	0.497
DBP (mmHg)	τ	24.4	0.9	24.8	3.8	0.812
	M	77.3	6.5	75.9	7.4	0.641
	A	8.6	2.9	9.8	3.9	0.570
	ϕ	15:13	1:10	15:48	1:14	0.420
HR (bpm)	τ	23.0	1.8	26.8 (116.8%)	4.8	0.089
	M	74.0	10.3	73.5	8.7	0.873
	A	7.6	5.5	9.4 (123.8%)	4.5	0.022
	ϕ	14:10	1:35	13:37	5:24	0.784
D (°)	M	3.576	0.254	3.598	0.28	0.324
	A	0.095	0.029	0.23 (243.5%)	0.08	0.008
H (nT)	M	11,026.1	26.04	11,006.3 (99.8%)	39.22	0.070
	A	40.28	58.56	93.0 (230.9%)	50.08	0.054
Z (nT)	M	51,956.0	55.89	51,952.9	46.23	0.645
	A	8.19	5.44	25.35 (309.6%)	12.98	0.012
Inc (°)	M	78.02	0.03	78.04	0.05	0.121
	A	0.041	0.06	0.10 (247.3%)	0.05	0.060
F (nT)	M	53,113.1	51.27	53,106.1	39.28	0.322
	A	15.32	10.58	24.13 (157.5%)	9.98	0.025

* Based on 48 h spans from ABPM records covering at least 5 days; geomagnetic indices from Tromso. SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate. Geomagnetic indices: D: declination; H: horizontal component; Z: vertical component; Inc: inclination; F: yotal field intensity. Circadian parameters: τ: period; M: MESOR; A: 24 h amplitude; ϕ: 24 h acrophase. *p*-values not corrected for multiple testing.

3.3. Biphasic (Hormetic) Response of SBP to Geomagnetic Stimuli

Two participants contributed 7-day/24 h ABPM records during the same span, which included days of moderate (column B in Figure 3), as well as extreme (column C in Figure 3), geomagnetic disturbances in addition to quiet days (column A in Figure 3). A biphasic response of SBP was observed, its circadian amplitude being increased during moderate geomagnetic activity but decreased during extreme geomagnetic activity, Table 3.

Such a hormetic reaction was found for SBP. Its circadian amplitude increased from 13.9 mmHg on quiet days to 21.4 mmHg (154.2%) on days of moderate geomagnetic activity but decreased to 10.6 mmHg (76.6%) on days of extreme geomagnetic activity ($p = 0.0044$). Geomagnetic activity was about 3 times higher on moderately disturbed days but about 12 times higher on extremely disturbed days compared to quiet days (Table 3).

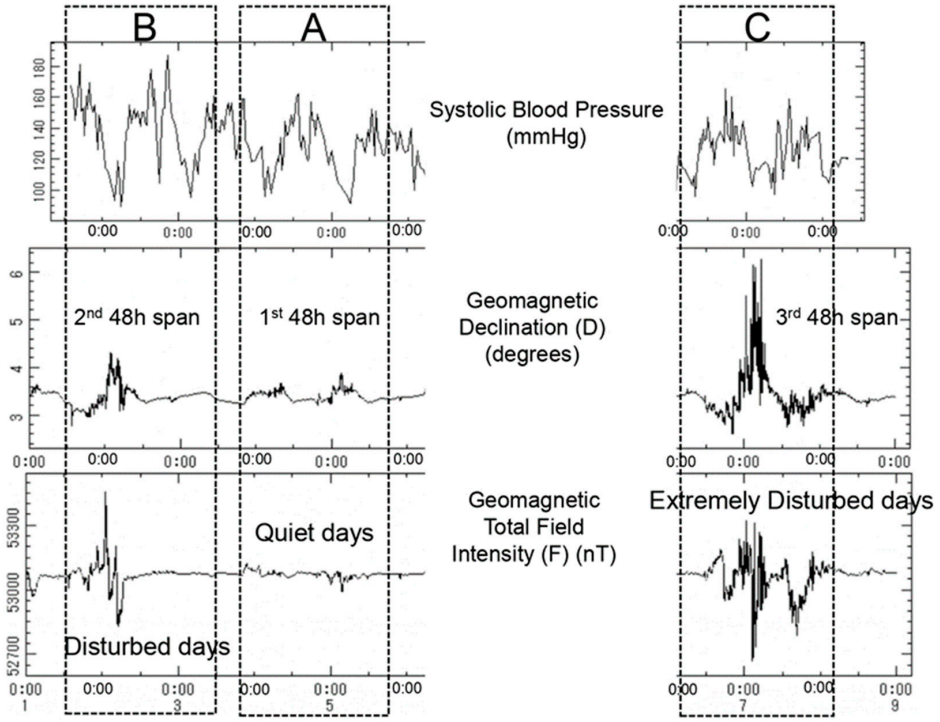

Figure 3. Illustration of SBP, geomagnetic declination, D (°), and total intensity, F (nT), in one study participant. (**A**): 48 h span during quiet conditions; (**B**): 48 h span during moderate geomagnetically disturbed conditions; (**C**): 48 h span during extreme geomagnetically disturbed conditions. The circadian amplitude of SBP is apparently increased during moderate geomagnetic disturbances (**B**) compared to geomagnetic quiet conditions (**A**), but it may be suppressed during extreme geomagnetic disturbances (**C**).

Table 3. Response of blood pressure and heart rate to moderate and extreme magnetic activity in 2 participants undergoing 7-day/24 h ABPM.

Variable (Circadian Parameter)		Comparison of Response of Circadian Profiles of BP and HR to Low- or Higher-Intensity Magnetic Stimulation											
		Quiet Days (Q) (n = 2)		Moderately Disturbed Days (MD) (n = 2)			Extremely Disturbed Days (ED) (n = 2)				Paired *t*-Test (MD vs. Q)	Paired *t*-Test (ED vs. Q)	Paired *t*-Test (ED vs. MD)
		Mean	SD	Mean	MD/Q (%)	SD	Mean	ED/Q (%)	ED/MD (%)	SD	*p*-Value	*p*-Value	*p*-Value
SBP (mmHg)	M	124.5	3.408	132.95		8.471	121.96			2.828	0.254	0.103	0.222
	A	13.9	1.937	21.38	(154.2%)	4.36	10.62	(76.6%)	(49.7%)	4.468	0.143	0.321	0.004
	ϕ	14:35	1:42	14:31		2:31	15:59			0:31	0.919	0.339	0.482
DBP (mmHg)	M	77.5	4.476	81.865		0.191	76.42			2.320	0.415	0.598	0.200
	A	9.9	3.80	12.07		2.065	10.83			0.078	0.357	0.798	0.538
	ϕ	14:35	14:09	14:55		1:39	16:15			0:58	0.844	0.195	0.605
HR (bpm)	M	66.0	14.602	65.06		4.469	65.62			11.95	0.921	0.887	0.933
	A	5.5	4.12	8.06		3.295	11.10			6.306	0.141	0.170	0.389
	ϕ	15:01	1:09	15:12		0:00	15:31			0:38	0.865	0.400	0.608
D (°)	M	3.370		3.361	(99.7%)		3.413	(101.3%)	(101.6%)				
	A	0.099		0.199	(199.8%)		0.436	(438.7%)	(219.6%)				
H (nT)	M	11,037.0		11,033.3	(100.0%)		11,011.6	(99.8%)	(99.8%)				
	A	15.62		58.86	(376.8%)		189.8	(1215.1%)	(322.5%)				
Z (nT)	M	51,904.4		51,906.6	(100.0%)		51,896.4	(100.0%)	(100.0%)				
	A	5.75		17.3	(300.9%)		66.68	(1159.7%)	(385.4%)				
Inc (°)	M	78.00		77.999	(100.0%)		78.020	(100.0%)	(100.0%)				
	A	0.016		0.062	(386.3%)		0.215	(1341.4%)	(347.3%)				
F (nT)	M	53,064.9		53,066.3	(100.0%)		53,052.2	(100.0%)	(100.0%)				
	A	7.49		21.63	(288.9%)		27.47	(367.0%)	(127.0%)				

SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate. Geomagnetic indices: D: declination; H: horizontal component; Z: vertical component; Inc: inclination; F: total field intensity. Circadian parameters: τ: period; M: MESOR; A: 24 h amplitude; ϕ: 24 h acrophase. *p*-values not corrected for multiple testing.

3.4. Circadian-Phase-Dependent Effect of Geomagnetic Stimulation on Circadian Amplitude of SBP and HR

Among the 16 study participants who underwent ABPM for at least 2 days, 10 (Group A: five men and five women, 35 to 51 years of age) saw geomagnetic stimulation start late during the day, between 14:00 and 20:00 (Figure 4, left). The other six (Group B: three men and three women, 20 to 55 years of age) saw it start in the morning, between 06:00 and 12:00 (Figure 4, right). Since changes in the circadian characteristics of BP and HR in response to geomagnetic activity may depend on the circadian phase at which geomagnetic disturbances start to occur in addition to the severity of the magnetic disturbances, results were compared between Groups A and B, Table 4. This chronomodulatory effect of geomagnetic stimulation consists of an amplification by 49.2% of the circadian rhythm in SBP ($p = 0.0003$) when geomagnetic stimulation starts in the evening, Table 4 (left). The MESOR of DBP is also statistically significantly decreased. But a morning start of geomagnetic stimulation is associated with an amplification by 38.0% of the circadian rhythm in HR ($p = 0.0596$), Table 4 (right). The MESOR of SBP is also slightly but statistically significantly increased from 118.1 to 121.8 mmHg ($p = 0.0285$).

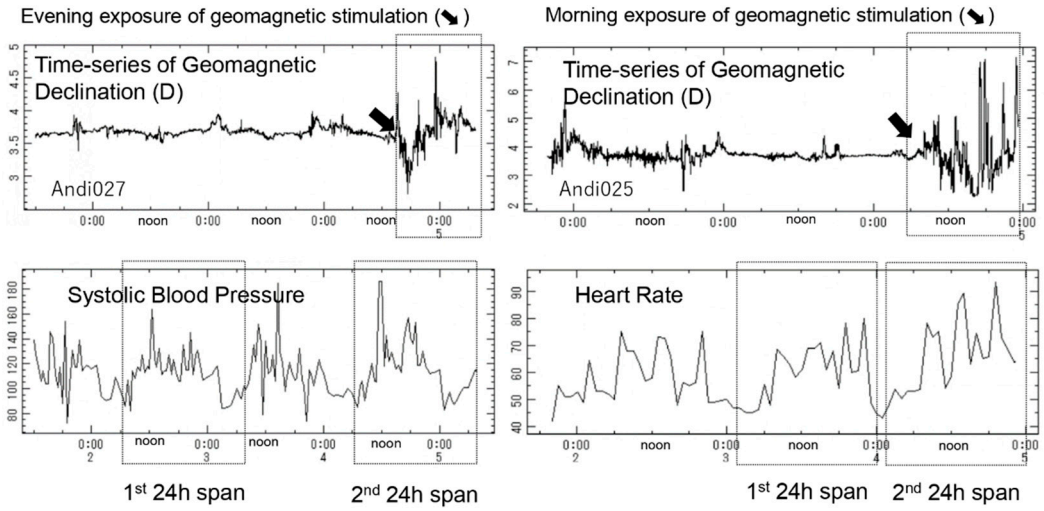

Figure 4. Response of the circadian amplitude of SBP (**left**) and HR (**right**) to geomagnetic stimulation starting either in the evening (**left**) or in the morning (**right**). Chronomodulatory effects of geomagnetic stimulation on the circadian amplitude of SBP (left) and HR (**right**) exist in clinically healthy individuals. When geomagnetic disturbances start in the evening, the circadian amplitude of SBP is increased ($p = 0.0003$, Table 4 left); when they start in the morning, the circadian amplitude of HR is increased ($p = 0.0596$, Table 4 right).

Table 4. Changes in BP and HR characteristics depend on the circadian phase at which geomagnetic stimulation starts.

		Group A (n = 10) (Geomagnetic Stimulation Started in the Evening: 14:00–20:00)						**Group B (n = 6) (Geomagnetic Stimulation Started in the Morning: 06:00–12:00)**					
		Quiet Day		**Disturbed Day**		**Paired *t*-Test**		**Quiet Day**		**Disturbed Day**		**Paired T-Test**	
		Mean	**SD**	**Mean**	**SD**	**t-Value**	***p*-Value**	**Mean**	**SD**	**Mean**	**SD**	**t-Value**	***p*-Value**
SBP (mm Hg)	M	120.82	8.19	118.65	11.15	−1.112	0.2951	118.09	12.59	121.80 (103.1%)	13.71	3.048	0.0285
	A	13.48	4.79	20.11 (149.2%)	4.12	5.683	0.0003	14.43	3.74	14.11	6.69	−0.100	0.9243
	ϕ	14:49	1:41	15:50	2:04	1.625	0.1385	15:39	1:28	16:54	2:25	1.177	0.2921
DBP (mm Hg)	M	75.14	6.47	71.21 (94.8%)	7.23	−3.379	0.0081	72.39	7.47	73.58	3.84	0.657	0.5401
	A	11.93	5.17	11.73	6.51	−0.087	0.9329	10.21	4.36	8.68	4.75	−0.467	0.6599
	ϕ	15:13	1:57	16:05	1:48	1.336	0.2144	14:53	2:05	14:17	5:28	−0.200	0.8495

Table 4. *Cont.*

		Group A (n = 10) (Geomagnetic Stimulation Started in the Evening: 14:00–20:00)						Group B (n = 6) (Geomagnetic Stimulation Started in the Morning: 06:00–12:00)					
		Quiet Day		Disturbed Day		Paired *t*-Test		Quiet Day		Disturbed Day		Paired T-Test	
		Mean	SD	Mean	SD	t-Value	*p*-Value	Mean	SD	Mean	SD	t-Value	*p*-Value
HR (bpm)	M	67.82	7.72	68.12	8.32	0.205	0.8419	66.21	6.57	68.5 (103.4%)	6.45	2.178	0.0813
	A	8.17	4.06	8.37	2.76	0.199	0.8468	8.64	3.60	11.92 (138.0%)	3.43	2.427	0.0596
	ϕ	14:51	2:54	14:15	4:12	−0.514	0.6199	13:21	1:38	15:37	3:43	1.257	0.2642
D (degrees)	M	3.615	0.182	3.666 (101.4%)	0.202	3.484	0.0069	3.711	0.201	3.728	0.211	1.471	0.2012
	A	0.092	0.060	0.202 (219.6%)	0.087	3.639	0.0054	0.083	0.044	0.152 (183.1%)	0.079	2.845	0.0360
	ϕ	9:22	9:46	4:16	6:25	−1.773	0.1100	5:46	8:50	5:58	8:40	0.034	0.9741
H (nT)	M	11,022.5	27.03	11,001.0 (99.8%)	31.50	−2.291	0.0477	11,017.3	26.38	10,991.2	54.09	−1.266	0.2612
	A	44.08	57.97	102.28 (232.0%)	59.34	3.692	0.0050	65.97	70.47	118.73	101.72	1.635	0.1629
	ϕ	15:09	4:55	13:15	2:19	−2.124	0.0626	15:18	3:46	12:51	4:25	−2.044	0.0963
Z (nT)	M	51,972.3	38.04	51,974.0	44.41	0.471	0.6490	51,994.9	42.10	52,002.3	47.96	0.810	0.4550
	A	14.72	11.46	37.32 (253.5%)	21.64	4.557	0.0014	21.02	20.44	57.23	72.68	1.148	0.3027
	ϕ	14:37	4:54	12:57	9:21	−0.483	0.6408	13:35	6:36	12:36	8:47	−0.212	0.8405
Inc (degrees)	M	78.03	0.03	78.05 (100.03%)	0.04	2.330	0.0448	78.04	0.03	78.07	0.06	1.273	0.2591
	A	0.045	0.064	0.112 (248.9%)	0.068	3.809	0.0042	0.068	0.076	0.135	0.119	1.734	0.1434
	ϕ	12:50	9:54	5:57	9:01	−2.454	0.0365	3:30	4:07	9:06	9:20	1.162	0.2976
F (nT)	M	53,128.4	34.95	53,125.7	41.65	−0.663	0.5242	53,149.4	39.32	53,151.6	41.15	0.307	0.7715
	A	17.14	7.52	31.52 (183.9%)	11.58	3.687	0.0050	25.58	24.07	40.83	57.65	0.543	0.6107
	ϕ	14:56	4:13	12:11	7:38	−1.202	0.2600	14:59	2:43	11:06	7:17	−1.060	0.3378

SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; D: geomagnetic declination; Inc: geomagnetic inclination; H: horizontal componnt; Z: vertical component; F: field intensity; *p*-values not adjusted for multiple testing.

4. Discussion

Mild geomagnetic disturbances, about twice as intense as geomagnetic activity on quiet days, amplified the circadian rhythm of SBP in clinically healthy citizens of a subarctic area located at a latitude of 70° N (Alta, Norway) and delayed the circadian acrophase of SBP and DBP (Table 1). Moderate geomagnetic disturbances, about three times more intense than quiet days, amplified the circadian amplitude of SBP and HR (Table 2). More severe geomagnetic activity, about twelve times more intense than geomagnetic activity on quiet days, however, weakened the circadian rhythm of SBP (Table 2). Even in the case of moderately disturbed days, the MESOR and circadian amplitude of SBP decreased with increasing geomagnetic activity, and the circadian acrophase of SBP was delayed, as shown in Figure 2.

4.1. Bell-Shaped, Typical of Biphasic, Response of Circadian BP Rhythm to Geomagnetic Stimuli

This study showed several effects of geomagnetic stimuli on human BP and HR. One of them is a hormetic (biphasic) response of BP to geomagnetic activity, which could represent an adaptive compensatory response to a novel environmental stress. In biology and medicine, "hormesis" is defined as a process in which exposure to higher doses of a given environmental factor is damaging, but it is beneficial at lower doses, when it can induce a beneficial adaptive effect on the cell or organism [76–84]. Of course, zero doses will not cause any beneficial biological effects because of a lack of adaptive responses at a subcellular, cellular, tissue, or clinical level.

Our previous investigations in Alta and in astronauts onboard the ISS support findings herein. The biphasic response observed in this study could be part of a broader bell-shaped dose-response curve wherein responses appear only in a certain range of stimuli or doses (so-called "windows"), as proposed by Murase [85] and/or at certain times, as proposed by Bawin and Adey [86]. The existence of a "window", whose width can differ individually, accounts for specific responses occurring strongly only under given circumstances. For example, the VLF-component of HRV increased in space [18,19] but was apparently suppressed in Alta [70–72,87] during a geomagnetically disturbed day, the extent of geomagnetic disturbances differing between the two sets of experiments. We now understand that the VLF-component of HRV is intrinsically generated by the heart itself [20,88]. As such, this component should be fundamental to health and well-being [18–20,69,89–92].

4.2. Circadian-Phase-Dependent Effect of Geomagnetic Stimulation

Apart from "hormesis", another noticeable result of our study is the distinctive effect of geomagnetic stimulation, which depends on the circadian phase at the time of its occurrence. When geomagnetic disturbances started to increase in the evening and during the night, the circadian amplitude of SBP increased ($p = 0.0003$), and the MESOR of DBP decreased ($p = 0.0081$). When geomagnetic disturbances started to increase in the morning and during the daytime, the circadian amplitude of HR increased ($p = 0.0596$), and the MESOR of SBP ($p = 0.0285$) and HR ($p = 0.0813$) increased. From the perspective of chronomedicine [2,27], a circadian-phase-dependent response to a stimulus such as environmental stress is referred to as "chronomodulation" [93–96]. Chronomodulation is defined as a process coordinated through multi-level interactions and accounting for the qualitatively as well as quantitatively different effects of the stimulus that are predictable insofar as they are rhythmic.

The response of a physiological variable to an external stimulus is modified in feed-sidewards mechanisms by other factors acting not only on the mean value but also on the rhythm's amplitude, phase, and/or period. Several cellular and molecular mechanisms have been shown to mediate chronomodulation [97–103]. The term "feedsidewards" has been used in a network of spontaneous, reactive, and modulatory rhythms [104,105]. For example, the response of bisected adrenals to ACTH is modified by the addition to pineal homogenate in rodents. In other words, the response of the adrenal (reactor) to the pituitary (actor) is modified by the pineal (modulator), which consists of enhancing the response when it is large and reducing it when it is small [93]. In our study, the BP response depends on the circadian phase when geomagnetic disturbances start increasing. Further discrepant results, conceivably associated with feedsidewards, are in need of more extensive studies to be tested longitudinally for much longer in a much larger number of individuals.

4.3. Role of Circasemidian Component Associated with Geomagnetic Fluctuations

Our previous investigation showed a more than doubling of the amplitude of the 12 h component of HRV indices in space [20]. The 12 h component has been reported in relation to the function of the "endogenous endoplasmic reticulum (ER) stress and unfolded protein response (UPR) cycle" [106–110]. It can be surmised to play an important role in adaptation to new environments, as humans start adapting to ER stress to survive. However, in this investigation, the circasemidian amplitude of SBP ($p = 0.0529$) and DBP ($p = 0.0606$) decreased (Table 1), suggesting that it responds only when faced with a harsh environment, such as space travel.

4.4. Rules of Procedure in Exploring Heliogeomagnetic Effects on Human Physiology

The magnetosphere is a vast cavity in which the Earth resides. It stems from the interaction between the geomagnetic field and the solar wind (a gas of charged particles flowing from the Sun) [29,111]. Life on Earth is protected by the atmosphere and the magnetic field. The Earth's magnetic field also protects the ISS from the space environment [111]. Biological effects thus result from exposure to weak geomagnetic fields from Earth and space [33,46,112–114].

As a function of solar cycle number, we found different HRV responses associated with geomagnetic disturbances: Our previous 2009–2016 studies (during solar cycle 24) on the ISS in space, the HRV (including TF, ULF, VLF, and LF components) response increased in seven clinically healthy astronauts [18,19]. Contrary to our 1998–2000 subarctic studies (solar cycle 23), HRV indices were suppressed in 19 clinically healthy individuals in response to magnetic storms, which involved larger magnetic disturbances than those observed in space [70–72].

HRV endpoints are hence affected by magnetic fluctuations in the magnetosphere, which enhance cardiovascular circadian rhythms, as shown herein. These effects bear on human health, well-being, and psychological resilience. Results from our studies on the ISS further suggest a possible anti-aging effect, probably mediated by the brain default mode network (DMN), in a light-dependent manner and/or with help from biological clocks [18–20]. This kind of information might lead to the formulation of new hypotheses and account for unanticipated results when accounting for the effects of magnetic storms that have an effect on the heart and brain, as we now learned. Concern for magnetic fluctuations entered programs on scientific chronobioethics for human health: the resonance of biological rhythms, brain plasticity, and psychological resilience. Further work on underlying molecular mechanisms, however, is warranted.

Several procedural rules in exploring chronobioethics are proposed:

(1) The atmosphere and the magnetic field provide protection on Earth [111]. Geomagnetic fluctuations in the magnetosphere significantly affect humans not only on Earth but also in space.
(2) Humans living at higher geomagnetic latitudes are particularly affected, as geomagnetic disturbances are stronger in arctic areas [55,71].
(3) Effects of geomagnetic disturbances on human physiology are nonlinear and display hormetic responses [72], perhaps understood as part of a broader bell-shaped dose-response curve [85]. Windowed responses appear only in a certain range of doses, which may differ among individuals and change depending on circumstances. They account for the lack of response outside, contrasting with a strong response inside these 'windows' [27–29,33,55,71,85,87]. Extremely high as well as extremely low geomagnetic activity seem to suppress BP or HRV variability and have adverse health effects [55].
(4) Decreases in HRV linked to geomagnetic storms, occurring more frequently when solar activity is high, reportedly increase cardiovascular risk in susceptible individuals. BP variability, on the other hand, is larger during solar minima and ascending solar cycle phases than during solar maxima, but storms during solar minima are more intense than those during solar maxima, perhaps accounting for changes in BP behavior along the course of the solar cycle [33,42].
(5) Effects of magnetic fluctuations on the activity of the brain's DMN are modulated by light and/or the circadian clock. Transcranial magnetic stimulation seemed to create a shift in the relationship between the medial prefrontal cortex and the dorsolateral prefrontal cortex, two nodes in the DMN [18–20,115].
(6) Geomagnetic stimulation at night improved sleep quality and induced slow-wave deep sleep not only on Earth but also in space. Geomagnetic disturbances also affect psychophysical processes. Their effects depend on individuals' sensitivity, health status, and capacity for self-regulation [18–20,46].
(7) Magnetic stimulation affect the period and amplitude of the endogenous circadian oscillation. These effects are circadian-phase-dependent, as they vary as a function of the time of day when geomagnetic activity occurs [116,117]. Increases in the circadian amplitude of HR and HRV suggest that the circadian system can be amplified in association with geomagnetic disturbances. The circadian amplitude of HR was also found to correlate statistically significantly with the 24 h, 12 h, and 8 h amplitudes of the geomagnetic declination index [19,20,118].

(8) Changes in the time-varying magnetic field above 80 nT over three hours significantly reduced melatonin concentrations in the body. Reduced concentrations of melatonin may play a role in the development of myocardial ischemia, as melatonin was found to improve myocardial microcirculation under laboratory conditions [119–122].
(9) Magnetic fluctuations can affect and enhance HRV indices involved in brain plasticity, psychological resilience, anti-aging effects, and longevity linked to the elevated activity of the brain's DMN with involvement by the circadian clock [19,20,52,112].

Recent evidence suggests that there might be an integrated signaling network in the brain's response to magnetic fluctuations [115,123–127]. This network could sense signals from the novel environment and in turn modulate the organism's response, probably in association with the brain's DMN and the circadian intrinsic timekeeping system, including sleep state, autonomic cardiovascular regulatory system, hormone synthesis, immune response, and metabolism.

Our studies suggested that humans have a light-dependent magnetoreception mechanism as an adapting mechanism involved in adaptive evolution in novel environments. These results led to our hypothesis of a possible involvement of clock genes (*Per2*, *Cry1* and *Bmal1*) [19,29,71,128].

A possible role of these clock genes (*Per2*, *Cry1* and *Bmal1*) in the response of cardiovascular variables to geomagnetic fluctuations was also suggested by others [129–137]. Kassahun et al. [116] reported that, when low-intensity magnetic stimulation was applied when PER2 expression is maximal, the circadian amplitude of PER2 increased by about 22% in in vitro SCN slices of PERIOD2::LUCIFERASE transgenic "knock-in" mice. When applied when PER2 expression was minimal, the circadian amplitude of PER2 expression decreased by about 17%, and the circadian period increased by 2.47 h as compared to controls. Effects of magnetic stimulation thus strongly depends on the circadian phase at which the stimulation is applied [116].

Lastly, a link between geomagnetic activity and human physiology and behavior has been suggested [33,43–46,128], including cardiovascular outcomes [138–142]. Our study on BP variability in a subarctic area, where the influence of geomagnetic disturbances is felt more strongly, adds to the already available body of evidence.

4.5. Limitations and Expectations for Future Investigations

This investigation has several limitations. First, the sample size is small, being limited to 16 participants. Second, even though 8 women are included, no information was available regarding their menstrual-cycle stage at the time of monitoring. Gonadal hormones are known to affect the response of the circadian system to light [143]; whether the menstrual cycle modulates the response to geomagnetic activity deserves further study. Third, several studies reported an interaction of geomagnetic disturbances and their latitude-dependence on the effect of melatonin on BP: apart from the role of melatonin on BP control, it reportedly has therapeutic uses on different pathologies of smooth muscles, including those related to gastrointestinal tract and urinary bladder instability [144]. Any involvement of melatonin in the hormetic response of SBP to geomagnetic activity or on its circadian-phase-dependence hence deserves further investigation. Finally, it will be important to understand the role human clock genes may play to facilitate hormetic and/or circadian-phase-dependent effects of geomagnetic activity on BP, as suggested by an in vitro SCN study [116].

5. Conclusions

To conclude, results herein indicate that mild, moderate, or extreme geomagnetic activity in Alta, Norway, induced changes in circadian rhythm parameters (amplitude, acrophase, and period) of BP or HR. Geomagnetic activity modulates their circadian variation in an intensity-dependent manner, perhaps as a bell-shaped windowed dose-response curve of functional and structural adaptations to the environment. As humans are currently suffering from several kinds of social jetlag, it is imperative that we learn

about chronobioethics [6,29,69]: the resonance of biological rhythms, brain plasticity, and psychological resilience, for a better health.

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Data Availability Statement: Due to the sensitive nature of the questions asked in this study, survey respondents were assured raw data would remain confidential and would not be shared.

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