Mobile Health Service is Promising to Detect the Blood Pressure and HRV Fluctuations Across the Menstrual and the Lunar Cycle

Alexander Meigal, Liudmila Gerasimova-Meigal, Alexander Borodin, Nina Voronova,
Liudmila Yelaeva, Galina Kuzmina
Petrozavodsk State University
Petrozavodsk, Russia
meigal@petrsu.ru

Abstract—**Here we report on experimental feasibility and preliminary results on mobile health services to detect enigmatic effect of the lunar cycle (LC) on heart rate variability (HRV) parameters and blood pressure (BP) in young females, with respect to the menstrual cycle (MC). We found that the MC exerted strong effect on varied HRV parameters specifically in the ovulation phase. Unlike the MC, the LC presented only tiny and non-significant, though still notable, effect on BP and HRV seen primarily in the full moon phase. We hypothesize on potential usability of e-medicine services, such as mobile-nested on-line day-to-day monitoring of electrocardiogram (ECG) for HRV, as a research tool for a longitudinal experiment with ultimate goal to detect the LC impact on human circulation system. Would such hypothetic effect experimentally been found, a mobile medicine services could be invented which allows user synchronizing the MC with the LC for better awareness on current physiological status and planning of daily activities and reproductive behavior.**

I. Introduction

Among public, there are long lasting believes about the lunar effects on human psychics, emotional status, and behavior [1]. Numerous studies attempted to document link between the lunar cycle (LC) and human activities, pathologies (e.g. epilepsy, mania), rate of birth, emergency calls, sleeping and waking strategies, tiredness and fatigue [2- 7]. As of now, among phases of the LC, full moon (FM) was reported as exerting the most effect on human behavior parameters, in particular, on sleeping [2], [7], [8]. Most of studies reported lack of significant main effects of moon phase on physiological parameters, while a few positive results were not further replicated [9]. Yet, no conclusive evidence of the LC effect on the human physiology was obtained. Such controversy with expectation that the LC still affects human organism ignited interest to the methodological issues of "lunar physiology". Most of "lunar" studies had i) across-subject design, and were ii) retrospective of former data sets [10]. As such, it was recommended to i) utilize a subject-oriented approach when one subject is examined several times throughout the lunar cycle (or several cycles) rather than across-subject design, and to ii) use hypothesis-driven approach with *a priori* expectations [10]. Additionally, it would be practical to enlarge list of physiological systems and corresponding parameters to be taken into LC studies.

Also, the menstrual cycle (MC) is rarely taken into consideration in the LC studies, though it has a similar circa-lunar period (28-29 days) and presumably has behavioral and evolutionary link with LC. Some studies support the idea that the MC interfere with the LC because men and women differently react on phase of the LC [5].

Women increasingly master professions and sports which earlier were attributed as merely "masculine", such as cosmonaut, military, boxing, weightlifting, football. Nowadays, many people are engaged in systematic health supporting activities (e.g. fitness, aerobic training, yoga, weight control). For women, knowing the effect of specific phase of the MC on neuromuscular and cardiac fitness may help them preventing excessive motor practices at that time with unwanted outcome. It is well acknowledged that the psychological status of women (depression, paranoidal thinking, decreased self-esteem), and their mental health and behavior is correlated with the MC phase [11-13]. In several studies it has been shown that heart rate variability (HRV) parameters are correlated with phases of the MC [14], [15]. We consider HRV as a reliable parameter that allow gaining insight into cardiovascular physiology and chronobiology of the man. To the best of our knowledge, no studies have been done on HRV under LC. Recently, we reported that HRV parameters, both linear and nonlinear, most strongly changed at the phase of ovulation of the MC, specifically in the spring season [16], [17].

We therefore hypothesize possible interaction between LC and MC in respect with HRV parameters in women. Based on earlier studies we expect that the combination of ovulation of the MC and the full moon of the LC presumably exert synergistic effect on HRV. According to recommendations of Cordi et al. [8] we utilized existing data sets on HRV collected at several points *longitudinally* from same individuals throughout the MC with synchronized day and phase of the LC. If that hypothesis holds, a smart medical service based on the mobile information and communication technologies can be designed to help women being aware of their current autonomic, reproductive and circulatory status. Additionally, a that could serve as powerful research tool which allows collecting current day-to-day data on HRV from one subject throughout the MC and LC within one year. This would have helped avoiding confounds arising from the across-subject studies and finally elucidating enigmatic influence of Moon on the human organism.

II. Subjects and methods

We made retrospection of the dataset on HRV collected by us in 2009-2011 (State Data Base Record #2014620775 of 28.05.2014, "Variability of heart rate", registered by Federal service on intellectual property of Russia). Twenty three healthy young females (aged 18-24 years, mean age ±SD was 19.9±1.4 years) have passed through all procedures. Their anthropological data on females can be obtained from Meigal et al. [17]. Electrocardiogram (ECG) was collected at 4 points of their menstrual cycle twice a year – in spring and autumn (Fig. 1). A total of 143 ECG samples were extracted from this data set locked with LC and MC phases, and further computed (Fig. 1). As such, the design of the study can be regarded as partially longitudinal.

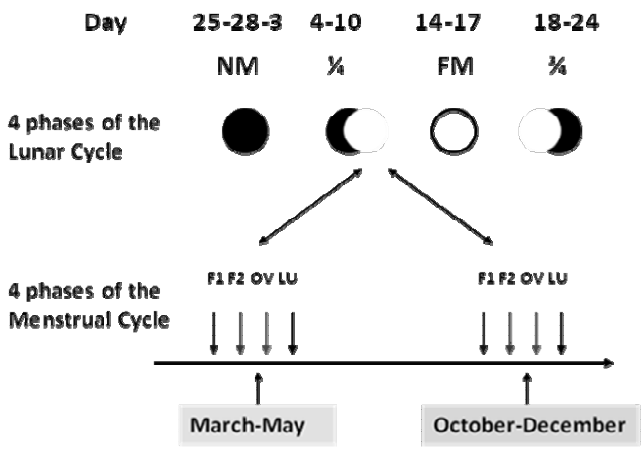

Fig. 1. Design of the study with points of data collection. NM – new moon, ¼ - waxing moon, FM – full moon, ¾ - waning moon. F1 – early follicular, F2 – late follicular, OV – ovulation, LU – luteal phase of the menstrual cycle

The ECG samples were collected with help of the VNS-Spectr device (Neirosoft Inc., Ivanovo, Russia) in the Lead II position within (5 min), between 10:00 and 12:00 AM in the morning to avoid inference of hormonal diurnal shifts; in a shadowed, deprived of noise room, at thermoneutral air temperature (20-22 °C), without preceding physical and emotional stress, not earlier than 1,5-2,0 hours after last consuming meals. Prior to ECG recording the subjects were allowed to quietly lay on a horizontal surface (medical bed) for 30 minutes to help get adapted and relaxed. The ECG was sampled under condition of quite breathing, in laying position. Subjects were asked to avoid swallowing saliva, coughing, and gasping.

A. Classification of Lunar phases

A phase of the LC was obtained from "Münchner Astro Archive" http://www.maa.mhn.de/StarDate/moonphases.htm. [6].

We classified the LC with distinction of the waning and waxing phases: new moon (25-28-3rd day, the darkest moon, 3 days around new moon, NM), waxing moon (4-10th day, growing moonlight, ¼), full moon (11-17th day, brightest moonlight, 3 days around full moon, FM), and waning moon (18-24th day, diminishing moonlight, 3/4).

Also, the lunar class was appointed: 1) lunar class 1 for the distance 0±4 days, 2) lunar class 2 for the distance 5±9 days and 3) lunar class 3 for the distance 10±14 days to the closest full moon [6]. In a way, lunar classes 1 and 3 corresponded with NM and FM from the above classification, while lunar class 2 appeared as a sum of with ¼ and ¾ phases, without respect to waxing or waning of the Moon.

B. Classification of phases of the menstrual cycle

Based on the individual basal temperature graphs, the early follicular phase (F1) was tested in average on the 7th day of the MC, the late follicular phase (F2) – on the 13th, the ovulation (OV) – on the 16th, and the luteal phase (LU) – on the 24th day of MC [16, 17]. Mean duration of the MC was 28,7±0,4 days. The ovulation phase was verified by daily measuring the basal body temperature (DT-520, A&D Company Ltd., Tokyo, Japan). Subjects had to map the temperature data in an individual graph. On this temperature graph, the first day of ovulation was defined as the first day of sustained temperature rise after basal body temperature nadir [17], [19]. In some cases, subjects had to rebuild their temperature graphs during the next MC due to uncertainty of the ovulation point. Mean values of the basal temperature through the MC in springtime and autumn are presented on Fig. 2.

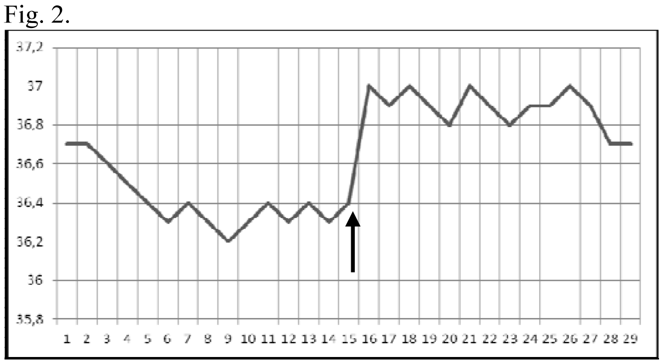

Fig. 2. Typical fluctuation of the basal temperature along the menstrual cycle in one of subjects. Arrows denotes ovulation

C. HRV and BP parameters

The arterial blood pressure (both the systolic – SBP, and the diastolic pressure - DBP) was monitored using a UA-705 device (A&D Company Ltd., Japan). Among the time-domain and frequency-domain HRV parameters, the following parameters were considered:

1) RRNN (ms) – mean interspike interval between neighbor RR interval; 2) RMSSD (ms) - root mean square of successive RR interval differences; 3) PNN50 (%) - percentage of successive RR intervals with difference bigger than 50 ms (PNN50, that is believed to depend on the respiratory cycle and, hence, on the parasympathetic nervous system); 4) high frequency (HF, Hz) spectral power characterizes RR variation at 0.15-0.40 Hz. It correlates with the respiratory cycle and may reflect the parasympathetic influence on HRV; 5) low frequency (LF, Hz) spectral power– spectral power characterizes RR variation at 0.04-0.15 Hz, that correlates both with the sympathetic and the parasympathetic influence on HRV; 6) very low frequency (VLF, Hz) spectral power characterizes RR variation at 0.003 до 0.04 Hz, that presumably reflects the hormonal inference (renin-angiotensin-aldosteron system, catecholamine, etc); 7) HF, % - the spectral power in HF band; 8) LF, % the spectral power in LF band; 9) TP (Hz) - all variation in RR interval within the measured frequency band.

Statistics was performed using the Statgraphics 15.0 Centurion software (Statpoint Technologies Inc., Warrenton, USA). The Mann-Whitney test (for pair comparisons), the Kruskall-Wallis test (for multiply comparisons), and two-way ANOVA were applied to validate effect of phase of the MC and the LC on the HRV and BP parameters.

III. RESULTS

A. Hemodynamic parameters (blood pressure)

SBP and DBP have not change throughout the MC, while the LC exerted a bit stronger, though still insignificant, effect on SBP and DBP (Fig. 3).

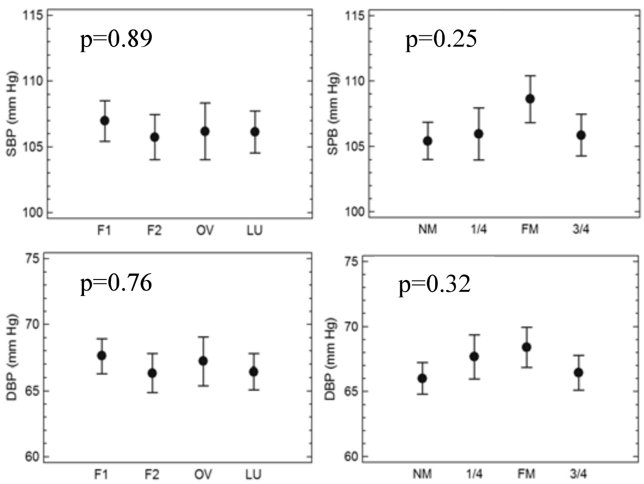

Fig. 3. The systolic (SBP) and diastolic blood pressure (DBP) across the menstrual (left column) and the lunar cycle (right column)

Two-way ANOVA allowed noting that DBP in ¾ phase of the MC changed specifically across the MC, while in other 3 phases of the LC the diastolic BP has increased in the ovulation phase. Nonetheless, the MC and LC did not significantly interact neither for SBP, nor for DBP (p>0.05) (Fig. 4).

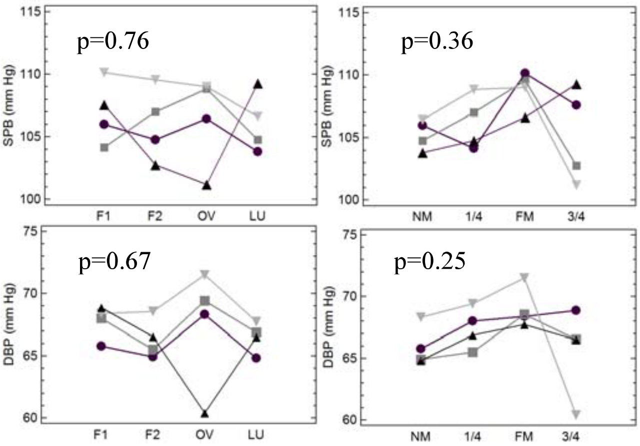

Fig. 4. The systolic (SBP) and diastolic blood pressure (DBP) across the menstrual (left column) with respect of the lunar cycle phase, and across the lunar cycle with respect of the menstrual cycle phases (right column)

In the left column: black filled circle is for NM, dark grey square – 1/4 , light grey down-triangle – FM, black up-triangle – for ¾. In the right column: black filled circle is for F1, dark grey square – F2 , light grey down-triangle – OV, black up-triangle – for LU.

B. The time-domain parameters of HRV

The values of the time-domain parameters of HRV (RRNN, pNN50%, and RMSSD) have significantly decreased specifically in the ovulation phase of the MC. In the LC, these have insignificantly decreased in the FM phase of the LC (Fig. 5).

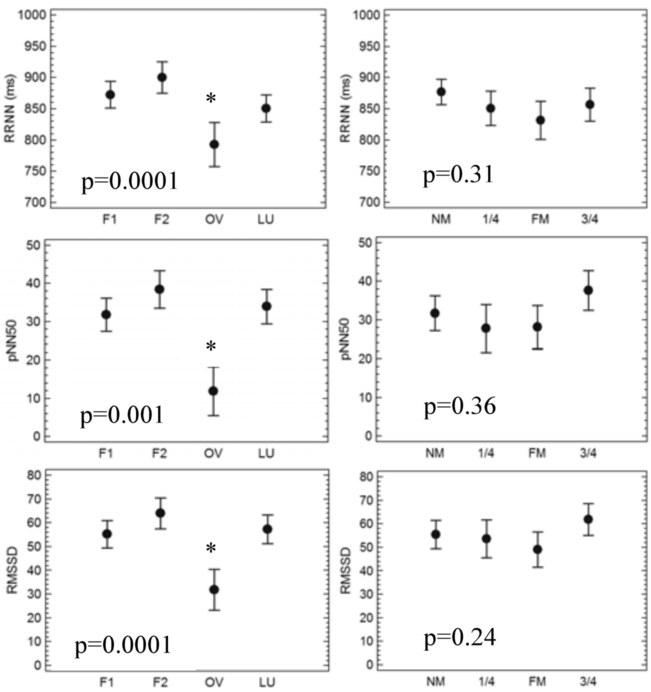

Fig. 5. The time-domain parameters of HRV across the menstrual (left column) and the lunar cycle (right column). * – p<0.05 difference of the ovulation phase to three other phases (ANOVA)

The LC did not impose influence (p>0.5) on the MC (Fig. 6, left) as in all phases of the LC the time-domain parameters of HRV fluctuated highly concordant across the MC. Across the LC, these parameters changed in a mode, specific to the phase of MC. Namely, in the phases F2 and OV the time-domain parameters have slightly decreased in the full moon phase, while in the F1 and LU that was not the case (Fig. 6, right). Still, this interaction was not significant (p>0.1). Amount of variance contributed by the MC to total variance was 11.7% for RRNN, 9.7% for RMSSD, and 13.8% - for pNN50. The LC did not contribute to total variance at all (far less than 1%).

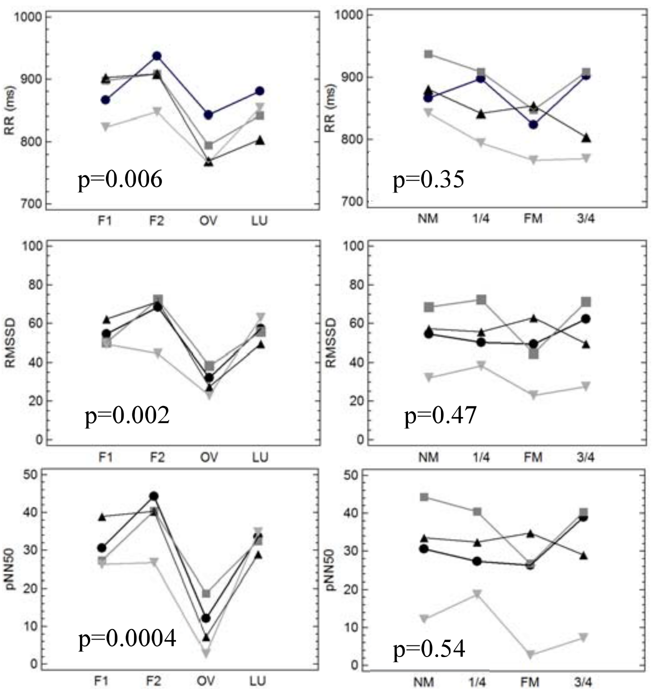

Fig. 6. The time-domain parameters of HRV across the menstrual (left column) with respect of the lunar cycle phase, and across the lunar cycle with respect of the menstrual cycle phases (right column)

In the left column: black filled circle is for NM, dark grey square – 1/4 , light grey down-triangle – FM, black up-triangle – for ¾. In the right column: black filled circle is for F1, dark grey square – F2 , light grey down-triangle – OV, black up-triangle – for LU.

C. The frequency-domain parameters of HRV

The TP has decreased, while VLF% has increased at the ovulation phase of the MC (Fig. 7). The HF%, correspondingly has decreased, and LF% did not change throughout the MC. Across the LC, these parameters have only slightly changed in the FM phase of the LC, though again insignificantly (p>0.5) (Fig. 8).

In all phases of the LC the frequency-domain parameters of HRV changed strictly concordant across the MC. As such, the LC has not interacted with the MC (Fig. 8) Throughout the LC, these parameters changed in a mode, specific to the phase of LC – TP and HF% has slightly decreased in the phases F2 and OV in the full moon phase, while in the F1 and LU phases that was not the case (Fig. 8, right). Yet, the effect of the LC on the MC was not significant (p>0.1). The VLF% did not present the MC on LC (Fig. 8). Amount of variance contributed by the MC to total variance was 6.9% for TP, 3.2% for VLF%, and 11.2% - for HF%. The LC did not contribute to total variance at all (far less than 1%).

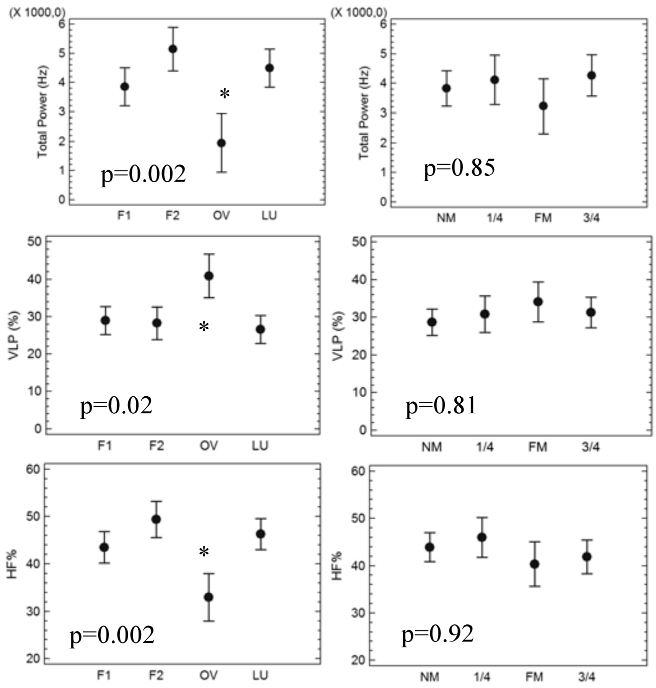

Fig. 7. The frequency-domain parameters of HRV across the menstrual (left column) and the lunar cycle (right column). * – p<0.05 difference of the ovulation phase to three other phases (ANOVA)

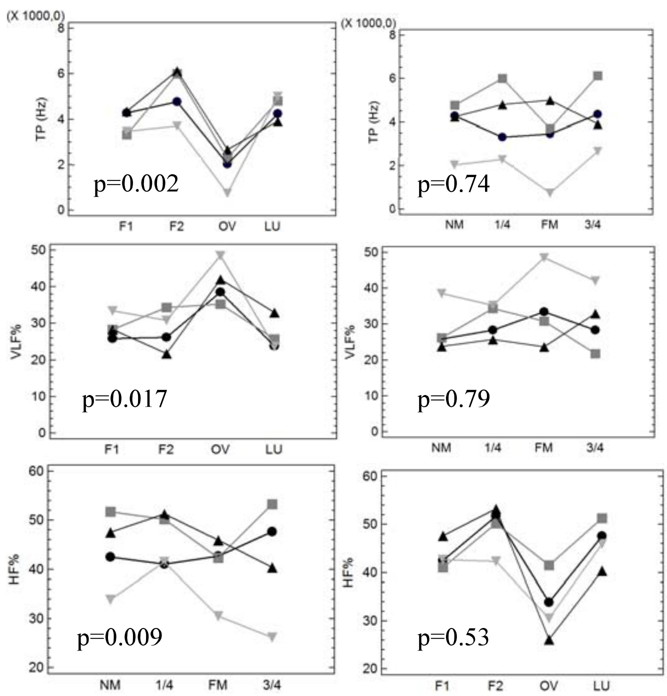

Fig. 8. The frequency-domain parameters of HRV across the menstrual (left column) with respect of the lunar cycle phase, and across the lunar cycle with respect of the menstrual cycle phases (right column)

In the left column: black filled circle is for NM, dark grey square – 1/4 , light grey down-triangle – FM, black up-triangle – for ¾. In the right column: black filled circle is for F1, dark grey square – F2 , light grey down-triangle – OV, black up-triangle – for LU.

IV. Discussion

The major hypothesis of the present study stated that the lunar cycle may have affected blood pressure and heart rate characteristics. Also, the study further explored the possibility of interaction of the lunar cycle with the menstrual one, which appears as natural human circa-lunar cycle. If this hypothesis holds, synchronization of definite phases of these two cycles would have produced specific effect on blood pressure or heart rate variability. The major outcome of this feasibility study was that the menstrual cycle exerts far stronger effect on most of HRV parameters in comparison to the lunar cycle. Though tiny and non-significant, the lunar cycle had influence on the HRV and blood pressure, in some instances approaching to significant values. By amount of contribution to total variance of studied parameters, we estimated that the MC outmatches the LC much more than 10 times.

As we earlier reported, the menstrual cycle exerts the most effect in the ovulation phase [16], [17]. More specifically, lower values of RRNN, pNN50, and RMSSD seen during the ovulation phase, evidence the decrease of the variability of heart rate. That, in turn, may be indicative of the weakened contribution of the parasympathetic nervous system in the net control of heart rate during ovulation [19]. Decrease of the power of high-frequency band indicates the same. Decrease of the total power of HRV spectrum reflects the general decrease of heart rate variability under ovulation, whereas growth of the very low frequency band power prompts increased contribution of the hormonal (neuro-humoral) factors in heart rate control [21]. Thus, one can assume that the hallmark of the HRV modification throughout the MC appears as growing inference of the sympathetic nervous system in cardiac regulation specifically during ovulation. This is in a good line with earlier studies, which have shown that the sympathetic activity prevails in the second (luteal) phase of the menstrual cycle [14], [15], [19]. In this study we have more precisely shown that such sympathetic hyperactivity starts at the ovulation phase. Presumably, this specific “sympathetic” bias of heart rate in the ovulation and, further, in the luteal phase may be associated with growing metabolism in women in the second part of the MC [20], that, in turn, could have been linked to their reproductive behavior [22].

In the *full moon* phase of the lunar cycle we observed similar, though weak and insignificant, tendency of HRV parameters and BP to shift in the direction of “sympathetic” aspect of autonomic regulation of heart rate. That was especially characteristic of the late follicular and ovulation phases of the MC. This allows further hypothesizing that the full moon and ovulation may exert synergistic, biologically equivalent effect on autonomic regulation. Physiologically, the full moon phase may mediate such effect via several possible mechanisms: 1) increased moonlight luminosity and, accordingly, decreased melatonin production [6], 2) impaired electromagnetic field of Earth [18], and 3) modified gravitational pull [7].

A. Implications for mobile medicine services

Though we utilized a partially longitudinal design in this study, still it was vastly based on the across-subjects protocol. Presumably, strong inference from different subjects prevented us from recording significant effect of the LC on BP and HRV. Enlarging data sets to hundreds or thousands subjects does not help [9]. We believe that only pure longitudinal study would help detecting enigmatic effect of the LC on human organism [9]. From clinical neurophysiology and signal processing it is known, that such small-amplitude events as, for example, nerve action potential during measuring of the sensory nervous conduction velocity needs hundreds repetitions of stimulus unless this action potential becomes visible among noise signals. We believe that repetition of several lunar cycles in a row in *one* individual may help revealing the LC effect on human circulation parameters.

As such, we assume that only a mobile medicine service would have helped collecting reliable longitudinal data on-line in day-to-day mode within one subject. If this project proved successful a mobile service could further be invented [23], which allows synchronizing the phase (or day) of the menstrual cycle with the lunar cycle phase (or day). The infrared sensor nested in the cell phone would have helped detecting ovulation to precisely monitor day of the menstrual cycle.

B. Do women really want that?

We assume it as very much likely. Knowing effects of the MC and the LC on specific functions of the organism would help planning daily activities, sports, hobbies and reproductive behavior in an on-line mode. Also, a male circa-lunar rhythm proved to be likely [24]. Therefore, male subjects could well have benefited from such study and mobile medicine service. Moreover, currently such approach to harvest data as crowd-tasking is coming more and more popular. It allows quickly collecting large-scale data with help of volunteers. Due to the advances in wearable technology, continuous registration of the health parameters became possible. Such easy-to-use personalized sensing devices provide the opportunity of the biosignal processing either on the local hardware, such as smart phones or tablets, or in the cloud. For this reason, the efforts of researchers are directed to the adoption of wearable health sensors in the healthcare services.

A number of electrocardiogram analysis algorithms are developed in our previous work within a CardiaCare project that is aimed at continuous monitoring of heart function in real-time and analyzing electrocardiograms on a smart phone [25]. Within the CardiaCare project the efforts are concentrated on timely detection of rhythm abnormalities. Despite the fact that the arrhythmias are harmless in general, they can pose serious threat of complications against chronic diseases such as hypertension or diabetes. Therefore, continuous heart rhythm monitoring provides the possibility to detect the deterioration of heart function and even to save the life. In this work, the mobile app was developed for day-by-day registering of ECG episodes and further extraction of R-R intervals on the base of CardiaCare application. R peaks are detected by means of the algorithm of Teager-Kaiser energy estimation, developed and analyzed before [26]. This approach unveils the opportunity of using the mobile devices and wearables in long-term clinical trials. On the one hand, having received initial instructions, participants of the control group are able to continue harvesting of the data completely independently. On the other hand, researchers receive the data as soon as they were obtained by remote participants. In general, a partially longitudinal design implemented in the present study did not help evidencing influence of LC on HRV. Thus, only strictly longitudinal study would have been helpful. Knowing that, we eager to launch a study in effort to reveal HRV fluctuations over long time (several months or a year) using a CardiaCare application [26] collecting data from several volunteers of both sexes in a day-to-day mode. HRV will be computed automatically based on on-line R-R intervals assessment.

V. CONCLUSIONS

In accordance with recommendations for studies in chronobiology, and especially for such problematic biological cycle as the lunar one, we applied partially longitudinal design to our study. Namely, we collected 8 samples of ECG across the menstrual cycle from each subject. Yet, we did not find firm evidence that the lunar cycle exert effect on autonomic regulation of the heart rate or on blood pressure. Still, the data obtained can be regarded as promising, because at full moon most of studied parameters had tendency to change, especially in the ovulation phase. In ideal, to detect this tiny "lunar" effect one should consider an on-line day-to-day monitoring throughout the whole menstrual cycle or, more reliable, several menstrual cycles in a row with help of the e-medicine technique. Therefore, we propose a mobile-nested monitoring of ECG usually used in search for extra systoles or paroxysm of tachycardia [23] to make evident the lunar influence on the human organism. Besides contributing to physiology of circulation and cardiac physiology, this would have helped to invent mobile-based services which allow synchronizing phases of the lunar cycle with the menstrual one. Presumably, coincidence of the ovulation phase with the full moon phase may have had the most stressful effect on the feminine organism. That would have strengthened awareness of women about their physiological status.

This study was financially supported by the grant of Russian Foundation for Basic Research (16-07-01289), and by the grant of Ministry of Education and Science of Russian Federation ("Organization of scientific work", # 761).

REFERENCES

[1] R.G. Foster and T. Roenneberg. "Human responses to the geophysical daily, annual and lunar cycles", *Curr. Biol.* Vol. 18, 2008, pp. R784-R794.

[2] C.L. Raison, H.M. Klein, and M. Steckler. "The moon and madness reconsidered", *J Affect Disord.* Vol. 53, 1999, pp.99-106.

[3] C. Della Monica, G. Atzori, and D.G. Dijk. "Effects of lunar phase on sleep in men and women in Surrey", *J. Sleep Res.* Vol. 24, 2015, pp. 687-694.

[4] M. Röösli, P. Jüni, C. Braun-Fahrländer, M.W. Brinkhof, N. Low, and M. Egger. "Sleepless night, the moon is bright: longitudinal study of lunar phase and sleep", *J. Sleep Res.* Vol. 15, 2006, pp. 149-153.

[5] M. Smith, I. Croy, and K. Persson Waye. "Human sleep and cortical reactivity are influenced by lunar phase", *Curr. Biol.* Vol. 24, 2014, pp. R551-552.

[6] C. Cajochen, S. Altanay-Ekici, M. Münch, S. Frey, V. Knoblauch, and A. Wirz-Justice. "Evidence that the lunar cycle influences human sleep". Curr. Biol., Vol. 23, 2013, 1485-1488.

[7] M. Zimecki. "The lunar cycle: effects on human and animal behavior and physiology", *Postepy Hig. Med. Dosw.* Vol. 60, 2006, pp.1-7.

[8] A. Sjödin, M.F. Hjorth, C.T. Damsgaard, C. Ritz, A. Astrup, and K.F. Michaelsen. "Physical activity, sleep duration and metabolic health in children fluctuate with the lunar cycle: science behind the myth". Clin. Obes. Vol. 5, 2015, pp. 60-66.

[9] M. Cordi, S. Ackermann, F.W. Bes, F. Hartmann, B.N. Konrad, L. Genzel, M. Pawlowski, A. Steiger, H. Schulz, B. Rasch, and M. Dresler. "Lunar cycle effects on sleep and the file drawer problem". Curr. Biol. Vol. 24, 2014, pp. R549-550.

[10] V.V. Vyazovskiy, and R.G. Foster. "Sleep: a biological stimulus from our nearest celestial neighbor?" Curr. Biol., Vol. 24, 2014, pp. R557-560.

[11] R. Brock, G. Rowse, and P. Slade, "Relationships between paranoid thinking, self-esteem and the menstrual cycle", *Arch. Womens Ment. Health.*, Vol. 19, 2016, pp. 271-279.

[12] K.E. Saunders KE and K. Hawton, "Suicidal behaviour and the menstrual cycle", *Psychol. Med,.* Vol. 36, 2006, pp. 901-912.

[13] E. Baca-García, C. Díaz-Sastre, J. de Leon, and J. Saiz-Ruiz, "The relationship between menstrual cycle phases and suicide attempts", *Psychosom. Med.* Vol. 62, 2000, pp. 50-60.

[14] A.S. Leicht, G.D. Hirning, and D. Allen, "Heart rate variability and endogenous sex hormones during the menstrual cycle in young women", *Exp. Physiol.* Vol. 88, 2003, pp. 441-446.

[15] N. Sato, S. Miyake, J. Akatsu, and M. Kumashiro, "Power spectral analysis of heart rate variability in healthy young women during the normal menstrual cycle", *Psychosom. Med.* Vol. 57, 1995, pp. 331-335.

[16] N. Voronova, A. Meigal, L. Yelaeva, and G. Kuzmina. "Heart rate variability in women during various seasons and phases of the menstrual cycle", *Human Ecology.* №2, 2015, pp. 20-26.

[17] A.Yu. Meigal, N.V. Voronova, L.E. Yelaeva, and G.I. Kuzmina, Electromyographic characteristics of women in different phases of the menstrual cycle, depending on season and type of autonomic regulation", *Human Physiol.* Vol. 40, 2014, pp. 97-104.

[18] W.B. Cutler "Lunar and menstrual phase locking", *Am. J. Obstet. Gynecol.*, Vol. 137, 1980, pp. 834–839.

[19] M. S. Tenan, R. M. Brothers, and A. J. Tweedell, A. C. Hackney, and L. Griffin, "Changes in resting heart rate variability across the menstrual cycle", *Psychophysiology,* Vol. 51, 2014, pp. 996-1004.

[20] A. Meigal, N. Voronova, L. Gerasimova-Meigal, L. Yelaeva, and G. Kuzmina. "Heart rate variability predicts the ovulation in young women: possible implications for mobile medicine services", *Proc. of the 18th conference of FRUCT association*, 2016, pp. 558-563.

[21] G.R. Sandercock and A. Brodie, "The use of heart rate variability measures to assess autonomic control during exercise", *Scand. J. Med. Sci. Sports*, Vol. 16, 2006, pp. 302-313.

[22] A. Salonia, M. Pontillo, R. E. Nappi, G. Zanni, F. Fabbri, M. Scavini, R. Daverio, A. Gallina, P. Rigatti, E. Bosi, P. A. Bonini, and F. Montorsi, "Menstrual cycle-related changes in circulating androgens in healthy women with self-reported normal sexual function", *J. Sex Med.,* Vol. 5, 2008, pp. 854-863.

[23] D.G. Korzun, A.V. Borodin, I.V. Paramonov, A.M. Vasilyev, S.I. Balandin. "Smart Spaces Enabled Mobile Healthcare Services in Internet of Things Environments" *International Journal of Embedded and Real-Time Communication Systems,* Vol. 6, 2015, pp.1-27.

[24] P. Celec, D. Ostatnikova, Z. Putz, and M. Kudela. "The circalunar cycle of salivary testosterone and the visual-spatial performance". *Bratisl Lek Listy. Vol.* 103, 2012, pp.59-69.

[25] A.V. Borodin, A. V. Pogorelov and Y. V. Zavyalova "CardiaCare. Mobile System for Arrhythmia Detection", in Proc. of 13th Conf. Open Innovations Association FRUCT, Petrozavodsk, Russia, 22-26 Apr. 2013, p. 186.

[26] A.V. Borodin, A. A. Rudenya. "A Study of Teager-Kaiser Energy Operator Pertinence for R Peak Detection in ECG Recordings", in Proc. of AINL-ISMW FRUCT, Saint-Petersburg, Russia, 2015, 9-14 Nov. 2015, pp. 144-146.