Heart Rate Variability in Kittens during Early Postnatal Ontogeny

M. M. Fateev, T. N. Nikolaeva, K. V. Dashichev, and N. V. Olendar

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 147, No. 6, pp. 609-612, June, 2009
Original article submitted October 22, 2008

Heart rate variability in awake kittens under resting conditions was studied during the following periods of postnatal ontogeny: newborn animals, 10-day-old animals (eye opening), 20-day-old animals (rise on the legs), and 30-day-old animals (control). Newborn animals were characterized by high activity of the sympathoadrenal system due to birth stress. The effect of stress factors increased in 10-day-old kittens, which was related to the start of functioning of distant receptors and delivery of new environmental information into the brain. The acquisition of upright posture and locomotion on the limbs were accompanied by activation of the vagus nerve in kittens. Significant changes in temporal, geometric, and spectral characteristics illustrate an increase in adaptability of the organism and possibility for independent living (particularly, by the 30th day of life).

Key Words: *heart rate variability; autonomic nervous system; postnatal ontogeny*

Evaluation of heat rate variability (HRV) is widely used in pediatrics as a tool for rapid and efficient diagnostics of the maturity of the autonomic nervous system [10,11,14,15]. These tests are of particular importance in preterm infants. Due to immaturity of the nervous system (various regions and conducting pathways), these children have reduced threshold of adaptation and are characterized by high mortality rate [4,7]. The development of methods for adaptation of newborns to novel conditions is an urgent problem. Model experiments on animals are required to solve this problem.

The kittens can be used as a model. These altricial animals can be used in studying the early postnatal adaptation of preterm infants.

Here we compared the parameters of HRV in kittens with various degrees of maturity (newborn animals; 10-day-old animals, eye opening; 20-day-old animals, rise on the legs; and 30-day-old animals, control).

Department of Normal Physiology, Department of Faculty Pediatrics with Propedeutics of Children Diseases, Yaroslavl' State Medical Academy, Russia. ***Address for correspondence:*** fateev52@mail.ru. M. M. Fateev

MATERIALS AND METHODS

Chronic experiments were performed on 10 kittens. Parameters of HRV were studied in the following period of early postnatal ontogeny: newborn animals, 10-day-old animals (eye opening), and 20-day-old animals (rise on the legs). The control group consisted of 30-day-old animals with well-developed physiological systems [13].

ECG was recorded on a 2-channel electrophysiological device connected to a computer (IBP PC Pentium II) through an L-CARD E-440 analog-to-digital converter (ADC). ECG was recorded in lead II for 4 min using L-GRAPH software (supplied with ADC). The kitten was placed in a special box. ECG was recorded after adaptation of the animal to a novel environment under resting conditions. The analysis and primary processing of ECG were performed with RRMatch software. The calculation and graphic presentation of HRV parameters were performed with CRGraph software [8].

For the analysis of HRV, temporal (HR, standard deviation of normal *R-R* intervals [SDNN], variation coefficient, and root mean square of successive differ-

0007-4888/09/1476-0676 © 2009 Springer Science+Business Media, Inc.

ences in *R-R* intervals [RMSSD]), geometric (variation range, mode, mode amplitude, stress index, scattergram area, and scattergram width-to-length ratio), and spectral parameters (low-frequency [LF] wave power, medium-frequency [MF] wave power, high-frequency [HF] wave power, total spectral power, relative power of LF waves, relative power of MF waves, relative power of HF waves, and vagosympathetic interaction index) were used [2]. Geometric parameters were calculated at a histogram increment of 10 msec. Ranges of the spectral analysis in kittens were similar to those in adult cats (LF, 0.02-0.07 Hz; MF, 0.07-0.20 Hz; HF, 0.2-0.8 Hz) [12].

The data were processed with Statistica 6.0 software. We calculated the arithmetic mean, root-mean-square deviation, error of the arithmetic mean, and Student's *t* test. The differences were significant at $p<0.05$.

RESULTS

Newborn kittens differed from 30-day-old animals (control) by all parameters of ECG (except relative power of MF waves; Table 1). HR, mode amplitude, stress index, relative power of LF waves, and vagosympathetic interaction index in newborn kittens were much higher than in control animals (by 1.1, 2.1, 6.4, 1.6, and 6.1 times, respectively). SDNN, variation coefficient, RMSSD, variation range, mode, scattergram area, scattergram width-to-length ratio, LF power, power of MF and HF waves, total spectral power, and relative power of HF waves in newborn kittens were lower than in control animals (by 3.0, 2.7, 3.9, 1.1, 10.1, 1.4, 4.6, 6.7, 22.9, 8.2, and 2.7 times, respectively). Therefore, newborn kittens were in a birth stress. The central type of regulation and sympathicotonia are observed in all mammals (including humans) under these conditions [1,4,9].

Ten-day-old kittens were characterized by a greater increase in HR, mode amplitude, stress index, relative power of LF waves, and vagosympathetic interaction index as compared to control animals (by 1.2, 2.5, 10.5, 1.8, and 7.0 times, respectively; Table 1). SDNN, variation coefficient, RMSSD, variation range, mode, scattergram area, scattergram width-to-length ratio, power of MF and HF waves, total spectral power, and relative power of HF waves in 10-day-old kittens were much lower than in control animals (by 2.5, 2.1, 5.5, 1.2, 13.8, 2.2, 4.2, 29.4, 5.9, and 3.9 times, respectively). There were no significant differences in the power of LF waves and relative power of MF waves between 10-day-old and 30-day-old kittens ($p>0.05$). These data indicate that the start of functioning of distant visual and auditory receptors and manifold increase in the flow of afferent information to the brain are accompanied by a greater stress response of the organism (as compared to newborn kittens). Newborn animals did not differ from 10-day-old kittens by test parameters of ECG. The above conclusion was derived from a 1.5-fold increase in the scattergram width-to-length ratio in newborn kittens compared to 10-day-old animals ($p<0.05$). Moreover, the LF power in 10-day-old kittens was higher than in newborn animals (by 1.5 times, $p>0.05$). The data indicate that activity of the hypothalamic—pituitary—adrenal system is increased during this period of postnatal development [5,6].

Differences were revealed between 20-day-old and 30-day-old kittens. HR, relative power of MF waves, and vagosympathetic interaction index in these animals were elevated by 1.1, 1.5, and 2.4 times, respectively. The mode, scattergram width-to-length ratio, HF power, and relative power of HF waves were reduced by 1.1, 1.4, 3.8, and 2.1 times, respectively (Table 1). These changes in HRV indicate that the initiation of locomotor activity in kittens is accompanied by an increase in sympathoadrenal function. It is probably related to the redistribution and increase in the flow of afferent impulses from vestibular receptors with the start of locomotor activity (*i.e.*, change in the orthostatic position).

Twenty-day-old kittens significantly differed from newborn animals and 10-day-old specimens by various parameters of HRV (Table 1). SDNN, variation coefficient, RMSSD, variation range, scattergram area, LF power, MF power, HF power, and total spectral power in 20-day-old kittens were higher than in newborn animals (by 2.5, 2.5, 2.3, 2.5, 5.0, 3.8, 6.4, 6.1, and 4.9 times, respectively). The mode amplitude, stress index, and vagosympathetic interaction index in 20-day-old kittens were lower than in newborn animals (by 1.6, 4.1, and 2.5 times, respectively). SDNN, variation coefficient, RMSSD, variation range, scattergram area, scattergram width-to-length ratio, LF power, MF power, HF power, total spectral power, and relative power of HF waves in 20-day-old kittens were higher than in 10-day-old animals (by 2.0, 1.9, 3.3, 1.9, 6.9, 1.6, 2.6, 4.0, 7.8, 3.5, and 1.9 times, respectively). The mode amplitude, stress index, relative power of LF waves, and vagosympathetic interaction index in 20-day-old kittens were lower than in 10-day-old animals (by 1.9, 6.7, 1.3, and 2.9 times, respectively). Therefore, the vagus nerve is activated in 20-day-old kittens. Vagal tone depends directly on the posture-tonic and antigravity reactions (acquisition of standing posture with forelimbs and hindlimbs) [1]. It should be emphasized that activity of the vagus nerve increases more significantly by the 30th day of life (Table 1).

Our results indicate that HRV in kittens reacts to critical periods of early postnatal ontogeny. High activity of the sympathoadrenal system in newborn

TABLE 1. HRV in Kittens at Various Stages of Earl Postnatal Ontogeny ($M \pm m$)

Parameter	Age of kittens			
	30-day-old (control)	newborn	10-day-old	20-day-old
HR, bpm	236.0±7.1	262.0±8.3*	273.0±4.7**	261.0±3.8*
SDNN, msec	20.710±2.965	6.870±0.779***	8.420±1.167**	17.080±1.944^{+++xx}
CV, %	7.980±1.135	2.990±0.381**	3.820±0.522**	7.390±0.823^{+++xx}
RMSSD, msec	15.540±2.956	4.040±0.738**	2.820±0.383***	9.330±1.454^{++xxx}
MxDMn, msec	101.10±11.72	33.00±3.96***	43.30±7.99***	82.0±6.8^{+++xx}
Mo, msec	253.90±7.96	232.00±8.03*	218.30±3.33***	227.00±3.27*
AMo, %	24.20±2.78	50.60±5.17***	59.80±7.56***	31.70±2.98^{++xx}
SI, arb. units	638.00±178.44	4090±855**	6690±2775*	993.80±202.48^{++xx}
EllSq, msec^2	9723±2947	966.30±290.06**	702.3±136.5**	4832±1266^{++x}
EllAs, %	41.00±4.65	28.40±3.33*	18.60±2.74^{***o}	29.00±3.09^{*x}
LF power, msec^2	36.030±11.728	7.790±2.463*	11.450±3.632	29.470±6.357^{++x}
MF power, msec^2	24.500±6.313	3.650±0.782**	5.790±1.678*	23.340±4.065^{+++xx}
HF power, msec^2	52.290±18.716	2.280±0.995*	1.780±0.428*	13.940±2.194$^{*+++xxx}$
TP, msec^2	112.820±35.554	13.72±3.39**	19.020±5.452*	66.750±10.963^{+++xx}
LF, %	31.5±4.4	50.90±5.31*	57.20±3.02***	42.40±2.77^{xx}
MF, %	23.30±3.15	32.10±3.92	31.10±2.52	35.7±2.9**
HF, %	45.20±6.56	17.00±3.42**	11.70±2.45***	21.90±2.86^{**x}
LF/HF	0.960±0.248	5.850±1.268**	6.680±1.189***	2.330±0.379^{*+xx}

Note. CV, coefficient of variation; MxDMn, variation range; Mo, mode; AMo, mode amplitude; SI, stress index; EllSq, scattergram area; EllAs, scattergram width-to-length ratio; TP, total spectral power. $^*p<0.05$, $^{**}p<0.01$, and $^{***}p<0.001$ compared to the control; $^{o}p<0.05$, differences between newborn and 10-day-old animals; $^{+}p<0.05$, $^{++}p<0.01$, and $^{+++}p<0.001$, differences between newborn and 20-day-old animals; $^{x}p<0.05$, $^{xx}p<0.01$, and $^{xxx}p<0.001$, differences between 10-day-old and 20-day-old animals.

and 10-day-old animals is related to birth stress. The observed changes in 10-day-old kittens are associated with the start of functioning of distant receptors and delivery of new information into the brain. The initiation of locomotion with the limbs in 20-day-old kittens is accompanied by the appearance and further increase in vagal tone. Significant changes in HRV illustrate an increase in adaptability of the organism, widening of the reaction norm, and possibility for independent living.

REFERENCES

1. I. A. Arshavskii, *Essays on Age Physiology* [in Russian], Moscow (1967).
2. R. M. Baevskii, G. G. Ivanov, L. V. Chireikin, *et al*., *Vestn. Aritmol*., No. 24, 65-87 (2001).
3. I. L. Elizarova, L. P. Sukhomova, E. V. Kanaeva, *et al*., *Akusher. Ginekol*., No. 7, 45-51 (1991).
4. *Neonatology. National Handbook* [in Russian], Ed. N. N. Volodin, Moscow (2007).
5. A. D. Nozdrachev, *Physiology of the Autonomic Nervous System* [in Russian], Leningrad (1983).
6. N. E. Ordyan, S. G. Pivina, and V. V. Rakitskaya, *Ros. Fiziol. Zh*., **88**, No. 8, 1003-1009 (2002).
7. *Handbook of Neonatology* [in Russian], Ed. G. V. Yatsyk, Moscow (2004).
8. E. V. Sal'nikov, M. M. Fateev, A. V. Sidorov, *et al*., *Byull. Eksp. Biol. Med.*, **144**, No. 10, 372-375 (2007).
9. V. N. Shvalev, A. A. Sosunov, and G. Guski, *Morphological Bases of Cardiac Innervation* [in Russian], Moscow (1992).
10. B. C. Galland, R. M. Hayman, B. J. Taylor, *et al*., *Pediatr. Res*., **48**, No. 3, 360-368 (2000).
11. N. P. Heragu and W. A. Scott, *Am. J. Cardiol*., **83**, No. 6, 1654-1657 (1999).
12. G. Mancia, G. Parati, P. Castiglioni, and M. Di Rienzo, *Am. J. Physiol*., **276**, No. 6, Pt. 2, H1987-H1993 (1999).
13. P. M. Masliukov, M. M. Fateev, and A. D. Nozdrachev, *Auton. Neurosci*., **83**, No. 1-2, 12-18 (2000).
14. S. K. Mehta, D. M. Super, D. Connuck, *et al*., *Am. J. Cardiol*., **89**, No. 1, 50-53 (2002).
15. Y. Sato, K. Ichihashi, Y. Kikuchi, *et al*., *Hypertens. Res.,* **30**, No. 7, 601-605 (2007).