

Heart Rate Variability of Preterm Neonates in the first postnatal weeks (ProMote study)

Theano Kokkinaki^a, Aristeidis Petrakis^b, Ioannis Kyprakis^b, Nicole Anagnostatou^c, Maria Markodimitraki^d, Theano Roumeliotaki^e, Manolis Tzatzarakis^f, Elena Vakonaki^f, Aristidis Tsatsakis^f, Haridimos Kondylakis^{b,g}, Eleftheria Hatzidaki^c

^a Department of Psychology, University of Crete, contact: kokkinaki@uoc.gr; ^bComputational Biomedicine Laboratory, FORTH-ICS; ^cDepartment of Neonatology/Neonatal Intensive Care Unit, University Hospital of Heraklion, School of Medicine, University of Crete; ^d Department of Preschool Education, University of Crete; ^eDepartment of Social Medicine, School of Medicine, University of Crete; ^f Laboratory of Toxicology, School of Medicine, University of Crete; ^gComputer Science Department, University of Crete

Background: Heart rate variability (HRV) describes the variation of time intervals between each subsequent heartbeat and assesses autonomic nervous system (ANS) maturation. The maturation of ANS needs at least 37 weeks of intrauterine development to reach a threshold value. Preterm infants are born at a time when their ANS is immature, especially the parasympathetic nervous system (PSNS). HRV metrics' analysis of premature neonates in a narrow time window ranging from the first days after birth to the 35th week of life provides restricted evidence of increase in the sympathetic and parasympathetic measures for prematures born after 32 weeks but not for those born prior to 32 weeks. We aimed to investigate the HRV metrics' trajectories of premature infants (gestational age: 28 to 36 weeks) in the course of the first postnatal days in order to track maturational changes of HRV metrics in transition from pre-to postnatal life.

Method: In a sample of 50 preterm neonates, three measurements for neonates' HRV measurements were carried out as follows: 1. within 24 hours after birth, 2. on the third to fourth postnatal day after birth, and 3. at 35-36 weeks postmenstrual age (only for premature neonates born before 35 gestation weeks). Calculated HRV features were based on time-domain indices, frequency-domain values and non-linear measurements.

Results: The correlation analysis revealed that certain HRV features, particularly time-domain and frequency-domain measures, showed positive associations with gestational age (GA) and postmenstrual age (PMA), indicating maturational trends in autonomic function. However, the strength and direction of correlations varied across different HRV domains, reflecting the complexity of neonatal autonomic development. Univariate regression confirmed these trends, showing that both GA and PMA were generally associated with increased HRV values, while preterm status was linked to reduced heart rate variability, supporting established findings of delayed autonomic maturation in preterm infants.

Conclusion: Preliminary results of the study confirm that HRV trajectories in premature neonates are influenced by gestational age at birth. These findings may serve as a reference for evaluating autonomic function and identifying at-risk neonates for developmental monitoring or intervention.