

# Effect of Anesthesia on Fetal-Maternal Heart Rate Variability and Coupling in Pregnant Mice and Fetuses

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Recently fetal mice models are frequently used to study human congenital diseases. In order to study fetal Heart Rate Variability (HRV) in utero anesthesia are required to immobilize mother mouse for surgical procedure. However maternal and fetal cardiovascular responses to anesthesia in mice have not been explored till now. Therefore, the aim of this preliminary study is to investigate the changes in maternal and fetal HRV [MeanHR, SDHR, RMSSDHR] as well as fetal-maternal heart rate coupling [ $\lambda$  for F1:M3~12; F=fetal(beat): M=maternal(beat)] measures during anesthesia. A total of 10 fetuses from 6 pregnant female mice type of C57BL/6J were used in this study. On day 17.5 of gestation, pregnant mice were anesthetized with subcutaneous ketamine (Ketalar 500 mg: 100 mg/Kg) and xylazine (Rompun Inj Solution 2% Bayer; 10 mg/Kg) and maintained with inhalational isoflurane (Forane AbbVie Inc. 0.5%, 260 ml/min). The fetal ECG recording system for embryonic mouse was explained in the previous study [Khandoker *et al.* IEEE (EMBC), 5257-5260, 2018]. ECG signals of pregnant mice and their fetuses were simultaneously recorded for 15 min and analyses were performed on 3 segments (P1-first 5 min, P2-second 5 min, P3-last 5 min). Results show that maternal MeanHR and RMSSDHR significantly ( $p < 0.05$ ) decrease from P1 to P3 ( $324.5 \pm 51.5$  bpm (P1) to  $296.3 \pm 61.4$  bpm (P3); and  $12.2 \pm 25.8$  bpm (P1) to  $6.6 \pm 15.8$  bpm (P3), respectively). Fetal MeanHR, SDHR and RMSSDHR decrease from P1 to P3 ( $100.2 \pm 39.5$  bpm (P1) to  $89.4 \pm 31.6$  bpm (P3);  $7.1 \pm 11.8$  bpm (P1) to  $2.1 \pm 5.4$  bpm (P3); and  $1.76 \pm 4.8$  bpm (P1) to  $0.65 \pm 3.0$  bpm (P3), respectively). No significant changes were found between P1 to P2 or P2 to P3. Also fetal-maternal  $\lambda$  patterns were unchanged which could indicate possibility of placental transmission of anesthesia to fetal circulation. These observations suggest that both parasympathetic and sympathetic nervous system activities was suppressed by anesthesia treatment.