Abstract

Nrf2 protects the lung from adverse responses to oxidants, including 100% oxygen (hyperoxia) and airborne pollutants like particulate matter (PM) exposure, but the role of *Nrf2* on heart rate (HR) and heart rate variability (HRV) responses is not known. We hypothesized that genetic disruption of *Nrf2* would exacerbate murine HR and HRV responses to severe hyperoxia or moderate PM exposures. $Nrf2^{-/-}$ and $Nrf2^{+/+}$ mice were instrumented for continuous ECG recording to calculate HR and HRV [low frequency (LF), high frequency (HF) and total power (TP)]. Mice were then exposed to either hyperoxia for up to 72 hr or aspirated with ultrafine PM (UF-PM). Compared to respective controls, UF-PM induced significantly greater effects on HR ($P < 0.001$) and HF HRV ($P < 0.001$) in $Nrf2^{-/-}$ mice compared to $Nrf2^{+/+}$ mice. $Nrf2^{-/-}$ mice tolerated hyperoxia significantly less than $Nrf2^{+/+}$ mice (~22 hours; $P < 0.001$). Reductions in HR, LF, HF and TP HRV were also significantly greater in $Nrf2^{-/-}$ compared to $Nrf2^{+/+}$ mice ($P \leq 0.01$). Results demonstrate that *Nrf2* deletion increases susceptibility to changes in HR and HRV responses to environmental stressors, and suggest potential therapeutic strategies to prevent cardiovascular alterations.