The Alteration of Neonatal Raphe Neurons by Prenatal-Perinatal Nicotine Meaning for Sudden Infant Death Syndrome

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Resumen

Nicotine may link maternal cigarette smoking with respiratory dysfunctions in sudden infant death syndrome (SIDS). Prenatal-perinatal nicotine exposure blunts ventilatory responses to hypercapnia and reduces central respiratory chemoreception in mouse neonates at Postnatal Days 0 (P0) to P3. This suggests that raphe neurons, which are altered in SIDS and contribute to central respiratory chemoreception, may be affected by nicotine. We therefore investigated whether prenatal-perinatal nicotine exposure affects the activity, electrical properties, and chemosensitivity of raphe obscurus (ROb) neurons in mouse neonates. Osmotic minipumps, implanted subcutaneously in 5- to 7-day-pregnant CF1 mice, delivered nicotine bitartrate (60 mg kg(-1) d(-1)) or saline (control) for up to 28 days. In neonates, ventilation was recorded by head-out plethysmography, c-Fos (neuronal activity marker), or serotonin autoreceptors (5HT(1A)R) were immunodetected using light microscopy, and patch-clamp recordings were made from raphe neurons in brainstem slices under normocarbia and hypercarbia. Prenatal-perinatal nicotine exposure decreased the hypercarbia-induced ventilatory responses at P1-P5, reduced both the number of c-Fos-positive ROb neurons during eucapnic normoxia at P1-P3 and their hypercapnia-induced recruitment at P3, increased 5HT(1A)R immunolabeling of ROb neurons at P3-P5, and reduced the spontaneous firing frequency of ROb neurons at P3 without affecting their CO2 sensitivity or their passive and active electrical properties. These findings reveal that prenatal-perinatal nicotine reduces the activity of neonatal ROb neurons, likely as a consequence of increased expression of 5HT(1A)Rs. This hypoactivity may change the functional state of the respiratory neural network leading to breathing vulnerability and chemosensory failure as seen in SIDS.

Palabras clave

Palabras clave de autor:perinatal nicotine exposure; sudden infant death syndrome; serotonin; serotonin autoreceptors; central chemoreception

KeyWords Plus:BRAIN-STEM ABNORMALITIES; MEDULLARY RAPHE; SEROTONERGIC NEURONS; CENTRAL CHEMORECEPTION; VENTILATORY RESPONSE; RAT-BRAIN; IN-VIVO; EXPOSURE; MICE; RECEPTORS

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