Chronic phenytoin treatment reduces rat carotid body chemosensory responses to acute hypoxia

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Ventilation is peripherally controlled by afferent activity arising from the peripheral chemoreceptors. In the rat, chemosensory activity is conveyed to the central nervous system through axons of neurons located in the nodose-petrosal-jugular-complex. These neurons have distinct electrophysiological properties, including a persistent Na+ current. Acute blockade of this current with phenytoin and other anti-epileptic drugs reduces normoxic chemosensory activity and responses to acute hypoxia. However, because anti-epileptic therapy is prolonged and there is no information on the effects of chronic phenytoin treatment on peripheral chemosensory activity, we studied the effects of long-lasting phenytoin treatment (~25 days) on afferent chemosensory activity, on a wide range of oxygen inspiratory fractions. Osmotic pumps containing dissolved phenytoin (166 mg/mL) or vehicle (daily flow: 60 µL) were implanted subcutaneously in male adult Sprague Dawley rats. At the end of the treatment, the animals were anesthetized and carotid sinus nerve activity was recorded in vivo. Afferent chemosensory activity in normoxia was not significantly different between control (71.2±2.2 Hz) and phenytoin treated (95.4±2.1 Hz) rats. In contrast, carotid body chemosensory responses to acute hypoxic challenges were markedly reduced in phenytoin treated rats, specifically in the lowest part of the hypoxic range (control 133.5±18.0 Hz vs phenytoin treated 50.2±29.4, at 5% FIO2). Chronic phenytoin treatment severely impaired the chemosensory responses to acute hypoxia, suggesting that long-term phenytoin treatment in patients may result in a reduced peripheral respiratory drive together with a reduction in the respiratory responses to hypoxic challenges. © 2016 Elsevier B.V.

Carotid body

Chemosensory activity

Peripheral ventilatory drive

Petrosal ganglion

Phenytoin

oxygen

phenytoin

acute disease

adult

animal experiment

animal model

Article

brain hypoxia

carotid body

controlled study

drug efficacy

hyperoxia

male

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rat

single drug dose

treatment response