Time Dependant Effects Of Mechanical Ventilation And Hyperoxia On Central Signalling Pathways In The Developing Lung Identified By Comprehensive Transcriptome Analysis

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Neonatal chronic lung disease (nCLD) exhibits significant structural alveolar and vascular defects and frequently occurs in susceptible babies born prematurely and treated with mechanical ventilation and oxygen-rich gas (MV-O_2). Little is known about the hierarchy of molecular and cellular events that drive nCLD pathophysiology in its early stages, resulting in serious health consequences for this significant patient population. By the use of a unique model of the disease and translation of the findings to human samples we demonstrate critical differential and common effects induced by MV and O_2. Whereas transcriptome analysis revealed a pronounced down-regulation of gene expression in the developing lung following mechanical ventilation in room air (MV-RA) for 2 hours,this down-regulation was abrogated by the additional application of oxygen (MV-O_2). After 8 hours of MV-RA the down-regulation was less pronounced and counteracted by an up-regulation in gene expression in the lung under the impact of MV-O_2. In contrast, hyperoxia (O_2) was associated with a significant up-regulation of gene expression after 2 hours that was ameliorated after 8 hours. By the use of confirmatory experiments in human samples we proof expression of key signaling cascades in the preterm lung undergoing ventilation and oxygen treatment. In summary, this study unravels the early effects of postnatal injury induced by MV and O_2 in the developing lung to foster future studies focusing on the explicit role of these genes in nCLD pathophysiology.

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