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**Title:** Progression of diaphragmatic fatigue during inspiratory muscle loading in normoxia and hypoxia

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**Body:** Diaphragmatic fatigue is known to occur during heavy inspiratory muscle loading (IML) in normoxia and is suggested to be increased in hypoxia. This study investigated the progression of diaphragmatic fatigue during IML in normoxia and hypoxia. In a randomized-controlled, single-blinded trial transdiaphragmatic pressure after magnetic stimulation of the phrenic nerves (P<sub>di,tw</sub>) was assessed every 45 seconds in 20 healthy subjects during standardized IML (60-80% of maximal inspiratory pressure) in normoxia and hypoxia. Lung volume correction was applied for all P<sub>di,tw</sub>. Twelve Subjects showed a reduction in P<sub>di,tw</sub> >10% in hypoxia during IML (i.e. fatigued). P<sub>di,tw</sub> at task failure in hypoxia was lower than in normoxia (3,30±1,02kPa vs. 4.01±0,99kPa p<0.05). During normoxia the progression of P<sub>di,tw</sub> followed an exponential decay while P<sub>di,tw</sub> linearly decreased during hypoxia (Figure). To conclude, P<sub>di,tw</sub> during IML featured different progressions during normoxia compared to hypoxia. While normoxia resulted in an early decrease followed by a leveling off, hypoxia resulted in a steady decrease and more pronounced fatigue.