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Title: Stage-dependent regulation of brain-derived neurotrophic factor and transforming growth factor-β1 in patients with COPD

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Body: Chronic Obstructive Pulmonary Disease (COPD) is characterised by complex inflammatory, neuronal and fibrotic changes. Brain-derived Neurotrophic Factor (BDNF) and Transforming Growth Factor-β1 (TGF-β1) are stored in alpha-granules of platelets. Serum BDNF and TGF-β1 are predominantly platelet-derived (released from platelets during serum preparation). BDNF is a key regulator of neuronal plasticity, whereas TGF-β1 is involved in tissue repair and emphysema pathogenesis. We have previously shown that serum BDNF but not TGF-β1 is elevated in asthma, correlating with disease severity. The present study aimed to investigate serum concentrations of BDNF and TGF-β1 in different stages of COPD compared to non-COPD controls. 63 patients with stable COPD (GOLD 2: n=22, GOLD 3: n=28, GOLD 4: n=13) and 17 age- and comorbidity-matched controls without COPD were enrolled. Serum levels of BDNF and TGF-β1 were measured using ELISA. Serum levels of BDNF and TGF-β1 were significantly elevated in all stages of COPD as compared to controls. Highest BDNF concentrations were found in GOLD stage 3 (with a trend towards a decrease in GOLD stage 4), whereas highest TGF-β1 serum levels were found in GOLD stage 4. In contrast to asthma, COPD appears to be characterised by increased concentrations of both BDNF and TGF-β1. Very severe COPD is associated with highest TGF-β1 concentrations, but relatively lower BDNF concentrations. We thus speculate that these findings might reflect a maximum of neuronal and inflammatory activity in GOLD stages 2 and 3, and a predominant activity of tissue remodeling factors in GOLD stage 4.