Alteration of adenosine receptors in patients with chronic obstructive pulmonary disease

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Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality worldwide. Adenosine acts through four distinct receptors to mediate pro- and anti-inflammatory effects. The primary aim of this study is to investigate the expression in peripheral lung parenchyma, the major site of airflow obstruction in COPD, using immunohistochemistry, radioligand binding and real time quantitative polymerase chain reaction. Adenosine receptors were analyzed in age-matched smokers with COPD (n = 14) and smokers with normal lung function (control group; n = 20). A_1, A_{2A}, A_{2B} and A_3 receptors were differentially expressed in peripheral lung parenchyma. The affinity of A_1, A_{2A} and A_3 receptors was significantly decreased in COPD patients compared with control group [$K_D(A_1)$ = 3.15 ± 0.19* versus 1.70 ± 0.14 nM; $K_D(A_{2A})$ = 7.88 ± 0.68* versus 1.87 ± 0.09 nM; $K_D(A_3)$ = 9.34 ± 0.27* versus 4.41 ± 0.25 nM; *p < 0.01] whereas their density was increased [Bmax(A_1) = 53 ± 4* versus 32 ± 3 fmol/mg protein; Bmax(A_{2A}) = 852 ± 50* versus 302 ± 12 fmol/mg protein; Bmax(A_3) = 2078 ± 108* versus 770 ± 34 fmol/mg protein; *p < 0.01]. The affinity of A_{2B} receptors was not altered but the density was significantly decreased in COPD patients compared with the control group (Bmax = 66 ± 5* versus 189 ± 16 fmol/mg protein; *p < 0.01). A significant correlation was found between the affinity and density of the adenosine receptors and forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) ratio, an established index of airflow obstruction. In conclusion, this is the first report showing the presence of adenosine receptors differentially expressed in lung parenchyma in COPD compared with control smokers. These novel findings strengthen the hypothesis of a potential role played by adenosine receptors in the pathogenesis of COPD.

ALTERED DISTRIBUTION, SIGNALLING AND FUNCTION OF A_1 AND A_{2a} ADENOSINE RECEPTORS IN THE BRAIN OF WAG/RIJ RATS WITH GENETIC ABSENCE EPILEPSY BEFORE AND AFTER THE DISEASE APPEARANCE

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Adenosine shows anticonvulsant properties in different types of epilepsy, but its role in absence seizures is still to be defined. Here, we investigated the distribution as well as the signalling pathways and function of A_1 and A_{2A} adenosine receptors in genetically absence epileptic Wistar Albino Glaxo/Rijswijk (WAG/Rij) rats compared with August Copenhagen Irish (ACI) rats, not prone to develop this kind of epilepsy. In WAG/Rij rats, the disease onset occurs after 2 months of age, due to generation of abnormal oscillatory rhythms within the thalamocortical circuitry, including the reticular (nRT), ventroposterolateral and ventroposteromedial thalamic nuclei as well as the frontoparietal somatosensory cortex. Our study, carried out in young (1,5 months) and adult (6 months) animals, i.e. before and after seizure occurrence, focussed on cerebral areas above mentioned in comparison with hippocampus, not involved in seizure triggering. Immunohistochemistry and Western Blot analyses showed a