Functional and morphological changes of human neutrophils after treatment with dopaminergic agents

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Polymorphonuclear leukocytes (PMN) are innate immune cells recruited to sites of injury or infection within minutes, where they can act as specialized phagocytic cells.
Recent evidences reveal that the immune system is closely linked to the central nervous system (CNS) and that dopamine (DA), a neurotransmitter in the CNS, defined as neuroimmunetransmitter, acts as a mediator between the two systems. Several lines of evidences were produced in the last decades about a dopaminergic modulation of the acquired immunity, while there is little data on the dopaminergic modulation of the innate immunity. The purpose of our work is to characterize the morphological and functional changes in human neutrophils after treatment with dopaminergic agents.
D_1-like (D_1 and D_5) and D_2-like (D_2, D_3 and D_4) dopaminergic receptor (DR) expression was analyzed by real time PCR and flow cytometry. Cell migration was measured by optic microscopy and quantified as the difference (Δ) between resting values and values induced by the different treatments. ROS produced by PMN were assessed by use of the redox-sensitive dye C-DCDHF-DA coupled to spectrofluorimetry. Cell morphology was assessed by transmission electron microscopy (TEM) and scanning electron microscopy (SEM).
DR mRNA were $D_4>D_5>D_1=D_3>>D_2$. Flow cytometric assay of DR showed that the percentage (%) of PMN positive for the different DR were respectively: 79-80% and 48-63% for D_1-like and D_2-like DR.
PMN migration induced by fMLP 0.1 μM was (mean±SEM) 9.4±1.9 μm. DA 1 μM reduced migration to 26.2±18.0% of fMLP-induced values (n = 5, $P<0.01$ *vs* fMLP alone). The effect of DA was mimicked by the D_1-like DR agonist SKF-38393 0.1 μM (22.3±6.4% of fMLP-induced values, n = 5, $P<0.01$ *vs* fMLP alone) and reverted by the D_1-like DR antagonist SCH-23390 1 μM (22.7±13.9%, n = 3, $P>0.05$ vs fMLP alone, and $P<0.05$ vs fMLP+DA). In addition, the fMLP-induced effects on cell migration was unaffected by the D_2-like DR agonist pramipexole 1 μM (data not shown).
ROS generation, measured as arbitrary units (AU), induced by fMLP was 302.8±124.1 AU. DA 1 μM reduced fMLP-induced ROS generation to 63.0±18.0% (n = 11, $P<0.01$ *vs* fMLP alone). The effect was mimicked by SKF-38393 0.1 μM (56.7±44.3%, n = 13, $P<0.01$ *vs* fMLP alone) but not by pramipexole 1 μM (data not shown). DA 1 μM prevented fMLP-induced morphological changes of PMN and this effect was antagonized by SCH-23390 1 μM.
DA exerts inhibitory effects on human PMN, possibly through D_1-like DR. Neutrophils are acquiring an increasingly important role in several pathological contexts, and understand the influences of the dopaminergic system on them could provide the basis for new therapeutic approaches.