Modulation of neutrophil functions by dopaminergic pathways

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Background: During inflammatory responses, polymorphonuclear leukocytes (PMN), are among the first cell types that can leave the microcirculation and enter into the inflammatory site.
Dopamine (DA) is an endogenous neurotransmitters belonging to the monamine catecholamine family, which acts through the activation of DA receptors (DADR). Dopaminergic pathways modulating immune responses have been investigated only recently and the evidences in literature regard the interaction between PMNs and DA are very few. We therefore decided to investigate the effects of DA on several human PMNs key functions, also because PMNs plays a fundamental role in inflammatory phenomena in diseases affecting the CNS.

Material and method: PMN were obtained from venous blood of healthy subjects. DADRs (mRNA level and membrane receptor expression), were analyzed respectively, by Real Time PCR and flow cytometry. Viability and apoptosis level were measured through ANX V/FITC flow cytometry. PMN migration was assessed by the Boyden chamber assay. Reactive oxygen species (ROS) were detected by spectrofluorimetry. IL-8 levels was detected through ELISA assay.

Results: PMNs showed detectable levels of mRNA of DADRs. PMNs expressed on their membrane all five DADRs. DA did not affect PMNs viability. Incubation with DA (30 min and 3 h) increased the percentage of cells in late phase of apoptosis only at 1 μM. DA did not affect spontaneous migration, whereas reduced fMLP-induced migration. The D2-like antagonist Haloperidol 1 μM did not affect the effect induced by DA on fMLP-induced migration. On the contrary, the D1-like antagonist SCH23390 1 μM induce a reversion of the effect of DA on fMLP-induced migration. DA did not affect spontaneous ROS generation but significantly reduced the fMLP-induced ROS production. The inhibition exerted by DA was not modified by preincubation with Haloperidol while was completely reverted by SCH23390. DA did not affect IL-8 production.

Conclusions: Human PMNs express all DADRs, both at mRNA level, and on their surface. We found that DA slightly increases apoptosis and modulate some key function like migration and ROS production and these effects seems D1-like receptors mediated. These findings could give the basis to further studies to assess the possible role of PMN in diseases characterized by inflammation not only in periphery, but also at level of CNS.