Effects of metallic Carbon Nanotubes *in vitro* and *in vivo*

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We explored *in vitro* the mechanisms regulating the interactions between metallic multi-walled-carbon nanotubes (MWCNTs) and brain derived rat microglia cells in order to investigate whether electrical properties of MWCNTs could affect brain cell function and phenotype. Moreover, we evaluated *in vivo* the effects of the same CNTs administered to rats by inhalation. We assessed the effects induced by annealed and highly electro-conductive MWCNTs (*a*-MWCNTs) on the viability and function of microglia cells from rat brain cortex and compared the results with those induced by as prepared not conductive MWCNTs (MWCNTs) and redox-active Double-Walled-Carbon-Nanotubes (DWCNTs). The CNT capacity to stimulate the release by the exposed cells of pro-and anti-inflammatory cytokines (IL-1β, TNF-α, IL-10, TGF-β, TBX_2, PGE_2, NO, iNOs) and neurotrophic factors (mNGF) was assessed. Metallic MWCNTs, besides not being cytotoxic, were shown to stimulate microglia activation, by increasing significantly in a dose-dependent way, the release of the pro-inflammatory molecules at 24hrs exposure . A shifting to a significant production of the anti-inflammatory cytokines and neuroprotective-neurotrophic factor mNGF by the same cells was observed at 48hrs exposure. The analysis of exposed cell morphology by confocal microscopy, showed a cell transition from M1 (classical activation) to M2 (alternative activation-acquired deactivation) phenotype more evident at 48hrs exposure . Alternative activation is closely associated with M2 genes that promote anti-inflammation, tissue repair, and extracellular matrix (ECM) reconstruction. The preliminary *in vivo* experiments confirmed these results showing a significant change of tissue markers of brain damage in diabetic rats after 4 days from metallic CNT inhalation. Our findings seem extremely important for evidencing the capacity of electro-conductive *a*-MWCNTs to modulate brain cell behavior and function towards neuro-protective effects.