Here, we present a hypothesised summary for the changes following trauma in the adult CNS, associated with a single lesion to the spinal cord (e.g. dorsal column cut) or with a combined lesion to DRG neurons (e.g. peripheral + central branch lesion). A) We believe that following a single insult in the CNS, multi-functional cells such as macrophages are activated with “detrimental” (red coloured) instructions to mount a well-controlled immune response. This often results in the release of pro-inflammatory cytokines and poor myelin clearance not only from phagocytic cells but also from oligodendrocytes, which also contribute to the failure of CNS axons to regenerate. B) In contrast, following a preconditioning lesion, factors such as: I) the facilitated entry of macrophage cells into the CNS prior to CNS lesion and II) DRG activation and upregulation of cAMP, RAGs and BDNF, contribute to the beneficial phenotypic ‘priming’ of these cells (blue coloured). These factors provide these multifunctional cells with appropriate phenotypic characteristics favourable to CNS regeneration, possibly by increasing their phagocytic properties, their secretion of growth promoting neurotrophic factors (e.g. BDNF) and their interaction with other immune (e.g. T cells) and non-immune cells (e.g. astrocytes).

BNB = blood nerve barrier, RAGs = regeneration associated genes