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Acute immune responses in the brain differ from responses in blood

Immune cells of the brain called microglia, appear to have been adapted to their vulnerable environment. They react less destructive to danger signals than their counterparts in the blood.

Microglia are the resident macrophages of the central nervous system (CNS). They are involved in virtually all disorders and diseases of the CNS. Macrophages are also present in the other organs, and we are more and more beginning to appreciate that the tissue environment can influence many responses of macrophages. During diseases such as multiple sclerosis both microglia as well as blood-derived macrophages may be found in the CNS, where they possibly have different roles. Our group is therefore characterizing these cell types and their acute responses.

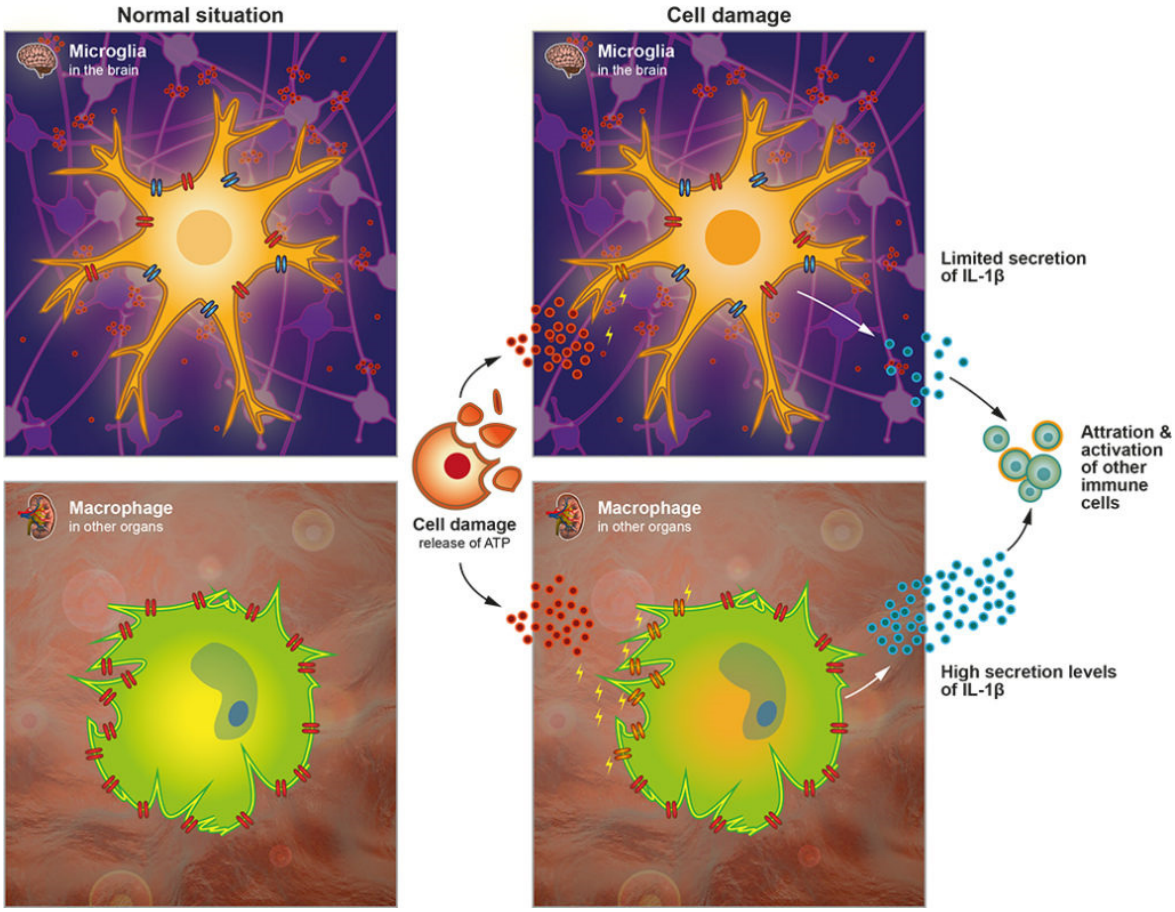

Fig. 1. Microglia reside in the CNS where extracellular ATP is present in the microenvironment under normal conditions. This in contrast to other tissue-resident macrophages. When cells become damaged and ATP is released from these cells as a danger signal, microglia respond less vigorously to this signal than other macrophages do. This is possibly an adaptation to their ATP-rich microenvironment to prevent inadvertent activation of the immune system.

In this research we focused on acute responses to ATP. High concentrations of ATP are released when a cell is damaged and thereby presenting a signal for “danger” to the surrounding (immune) cells. Both microglia and macrophages have specific receptors that detect ATP. Upon detection, the cells secrete a substance called IL-1β, which potently activates other immune cells.

We show that when exposed to ATP, microglia secrete much less IL-1β than other macrophages. We also revealed that microglia use different receptors to detect ATP than other macrophages do. The low secretion levels of IL-1β were most probably due to lower expression levels of a specific receptor on the surface of microglia as compared to other macrophages.

This phenomenon might reflect an adaptation of microglia to their microenvironment. In the brain, microglia are often exposed to high levels of extracellular ATP, since ATP is also important for the signaling between different nerve cells. The limited responsiveness of microglia to ATP might prevent inadvertent production of IL-1β in the vulnerable brain environment.

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ATP-induced IL-1β secretion is selectively impaired in microglia as compared to hematopoietic macrophages.
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