Interleukin-1β in Neuroinflammation associated to Alzheimer disease

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Introduction

Aims

- The main objective of this study consists in to obtain an overview of the neuroinflammation involved in Alzheimer disease.
- Considering several perspectives rely on a wide range of experimental models, to discuss whether a neuroinflammatory mediator which takes part on pro-inflammatory mechanisms, acts as a one of principal responsible in pathogenesis associated to Alzheimer disease.
- Get to know the processing and regulation of interleukin-1β throughout NLRP3 inflammasome assembly. Otherwise, treatments for Alzheimer disease by inflammasome inhibition are proposed.

Methods. Literature search of papers in databases like Pubmed restricting to Alzheimer disease, neuroinflammation, interleukin 1β and NLRP3. In addition, information found in scientific journals that contains the topic treated. Finally, selection of the most relevant papers and its treatment to write the discussion.

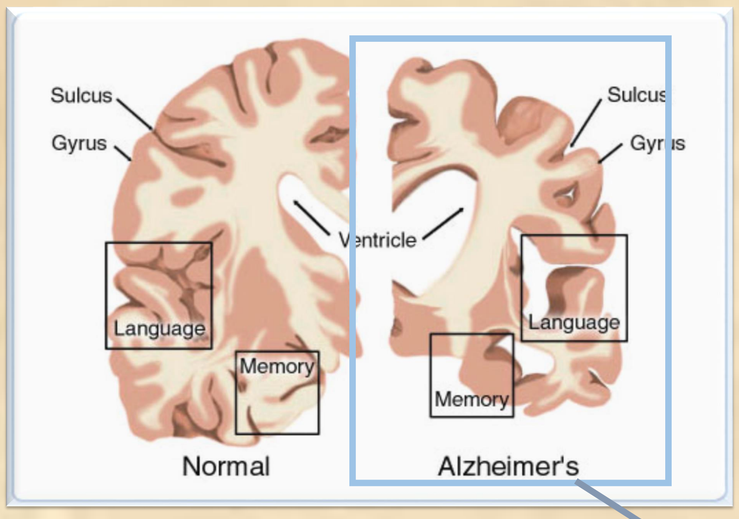
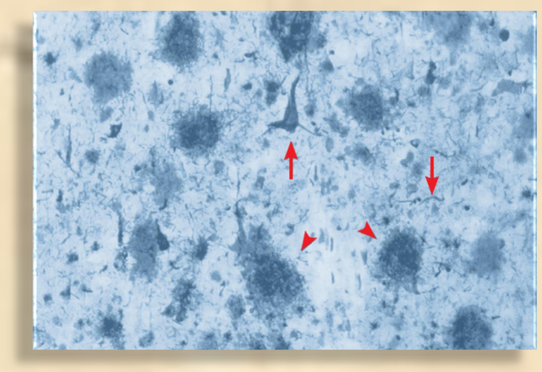


Fig.1 Neuropathology in Alzheimer Disease. Plaques Aβ arrowheads, neurofibrillary tangles arrows 15.1 La Enfermedad de Alzheimer. 2011, April 14 Retrieved May 31, 2015, from OCW Universidad de Cantabria Web site: http://ocw.unican.es/ciencias-de-la-salud/biogerontologia/materiales-de-clase-1/capitulo-15.-neurodegeneracion-y-aportaciones/15.1-la-enfermedad-de-alzheimer-1.



Results and Discussion

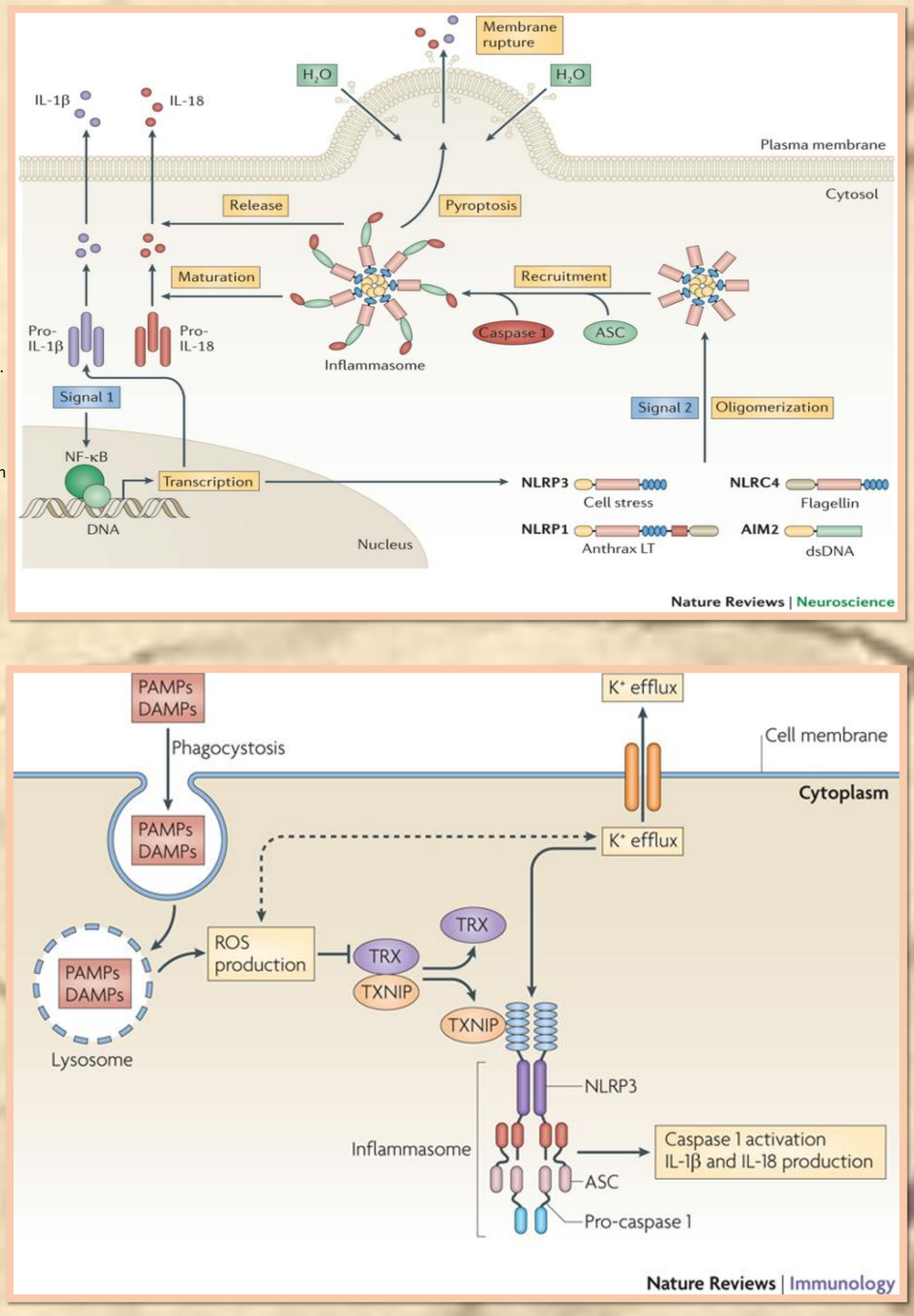


Fig. 2 Inflammasome Activation. John G. Walsh, Daniel A. Muruve, Christopher Power. Inflammasomes in the CNS (2014). *Nature Reviews Neuroscience* 15, 84–97

Fig. 3. Model of ROS to Inflamasome activation. Jurg Tschopp& Kate Schroder. NLRP3 inflammasome activation: the convergence of multiple signalling pathways on ROS production? (March 2010*) **N**ature Reviews Immunology 10, 210-215*

Interleukin- 1β, NLRP3 inflammasome, Alzheimer disease:

- Signal 1:
  Inmature Pro-IL-1β is transcribed throughout NF-kB factor.
- Signal 2:
  There are some factors which active the NLRP3 inflammasome. assembly such as ROS production or K+ efflux.
  NLRP3 oligomeration serve as a platform to caspase -1.
  Caspase-1 lets the maturation of pro-IL-1β into IL-1β.
- IL-1β is released by microglial cells due to the interaction with seniles plaques. The continuos production of citoquines triggers a high levels of neuroinflammation that contributes to patology.

Image: http://medicablogs.diariomedico.com/jena/page/58/

Conclusions

- Neuroinflammation is necessary to maintain homeostasis by the protection against external and intrinsic factors that could cause damage. On the other hand, under high activation or extended time, it becomes injury.
- It is well known that, immune responses are mechanisms tightly correlated. So, it is difficult to describe all process involved in neuroinflammation. Then, how the response in patients with Alzheimer is carry out has been wide studied and is still in developing.
- Interlequin-1β seems to be the key mediator in Alzheimer disease. Some evidences show raised levels of Interleuquin-1 β in conditions of pathology. The interaction with Aβ and microglia increase this citoquines and results in neuroinflammation.
- The assumption that NLRP3 and caspase-1 should be coexpress for IL-1 β production is shown in some experiments. These mediators act indirectly in neuroinflammation. It is the reason for new treatments with its inhibition have been tested.
- The huge variability in organisms and between them cause difficulties for pathogeny investigators. Moreover, found a new treatment is not easy because of elevated interconexion in the inmune responses. Some pro-inflammatory inhibitors require more studies to be used as a treatment to in the future.

Featured References:

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