

## Persistent ventriculomegaly in hydrocephalic rat brains: neuroinflammatory response

Funmilayo Olopade<sup>1</sup>, Temitayo Shokunbi<sup>1,2</sup>, Idris Azeez<sup>3</sup>, Anna Andrioli<sup>3</sup>, Ilaria Scambi<sup>3</sup>, Marina Bentivoglio<sup>3</sup>

1 Department of Anatomy University of Ibadan, Ibadan, Nigeria

2 Department of Neurosurgery, University of Ibadan, Nigeria

3 Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Italy

funmiolopade@yahoo.com

Hydrocephalus is especially prevalent in countries with limited resources, where its treatment is still a challenge. However, long-term neuropathological changes in untreated hydrocephalus largely remain to be explored. The present study examined whether neuroinflammation persists in acquired, chronic hydrocephalus. Intracisternal kaolin injections were performed in 3 week-old rats, followed by 1, 4 and 8 weeks survival. Ventriculomegaly has been previously reported to stabilize by the third week in this model. Matched control rats received saline injections. Single and triple immunocytochemical approaches were used to visualize astrocytes, microglia, and the pro-inflammatory cytokine interleukin (IL)-1beta in the parietal cortex, pursuing cell counts and densitometry. Microglial protein ionized calcium binding adaptor molecule 1 (Iba1) and IL-1beta expression was monitored with Western blotting in the parietal cortex and hippocampus. In the cortex, which showed progressive disruption of cytoarchitecture, neuronal cell density was significantly increased at 8 weeks post-induction but not at earlier time points, indicating ongoing cortical damage in chronic hydrocephalus. Astrocyte and microglia hypertrophy and quantitative analyses indicated sustained glial cell activation with a trend that persisted at 8 weeks. Iba1 expression showed at 4 weeks an increase that persisted at 8 weeks. IL-1beta expression peaked at 4 weeks and was then down-regulated. Overall the findings indicate that neuro-inflammatory features build up in the first month after hydrocephalus induction implicating marked IL-1beta up-regulation, and show that astrocyte and microglia activation persists in the presence of ventriculomegaly. The data also show that astrocytes are the main source of IL-1beta in this disorder.