The effect of the novel TSPO ligands 2-Cl-MGV-1 and MGV-1 on LPS-induced microglial activation

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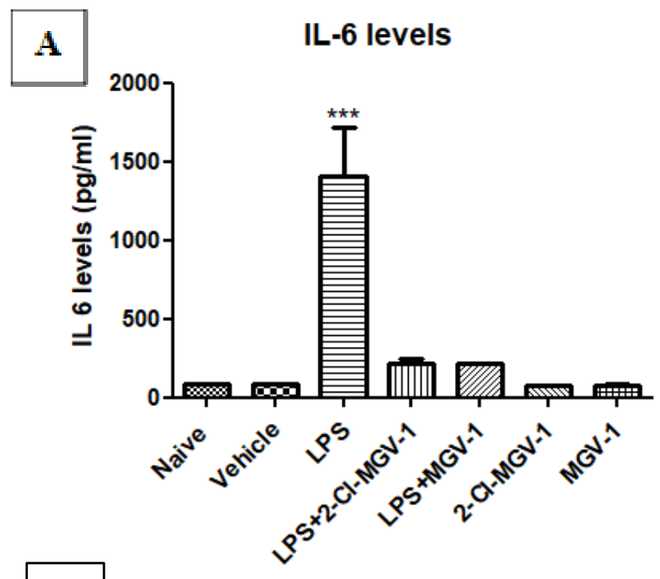
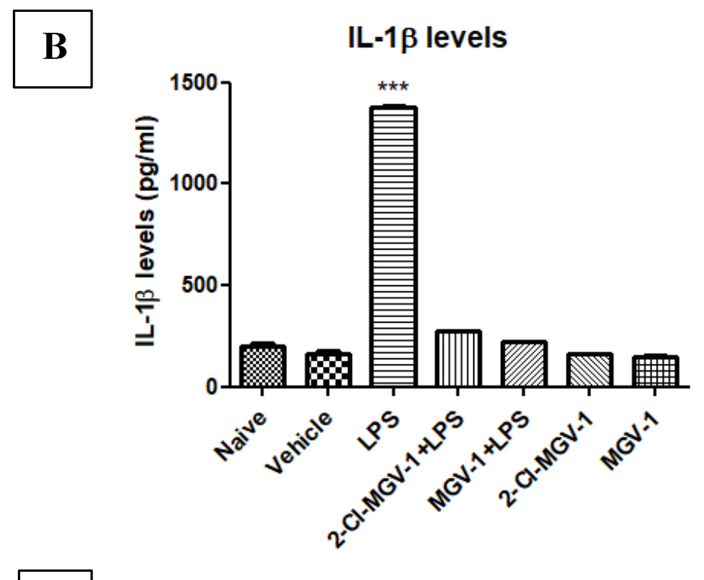
Implications of 2-Cl-MGV-1 and MGV-1 in microglial cell culture model

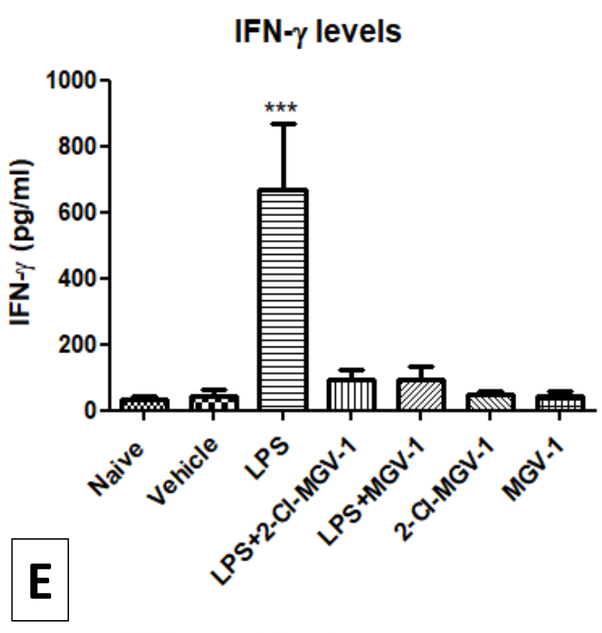
Protection against cell death of astrocytes
Reduction of microglial activation
Differentiation of neuronal type cells
Mitigation of neuronal cell death

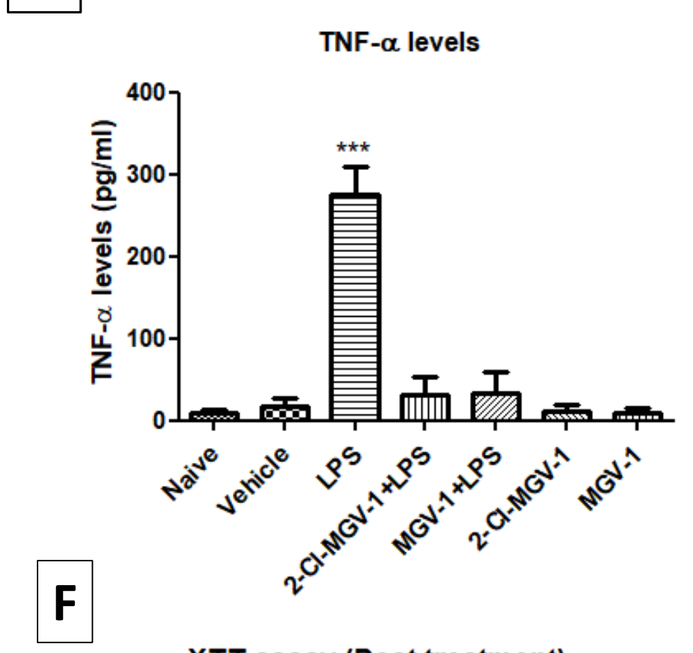
Introduction

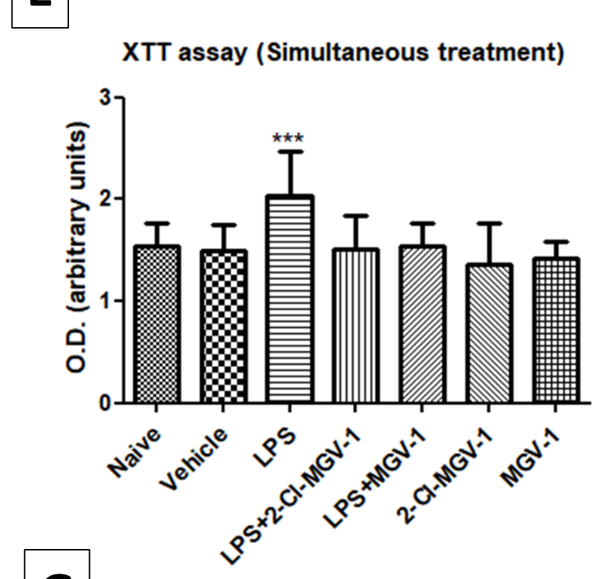
- TSPO is formerly known as the peripheral-type benzodiazepine receptor (PBR).
- TSPO was originally found in peripheral organs and tissues, and also in CNS non-neuronal cells.
- TSPO can be found throughout the body, but is particularly abundant in steroids producing tissues,
- TSPO levels typically are enhanced in association with injury and disease, in the brain and other tissues.
- M1 macrophages have the unique ability to metabolize arginine to the "harmful" molecule NO, whereas M2 macrophages can metabolize arginine to the "repair" molecule ornithine

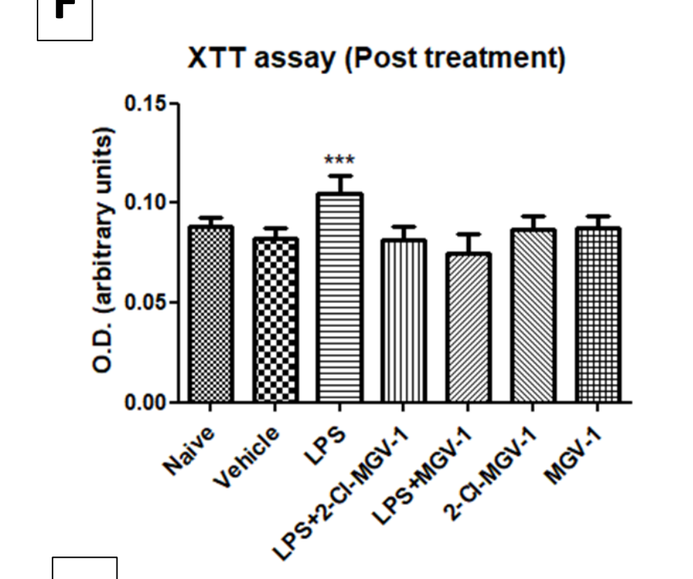


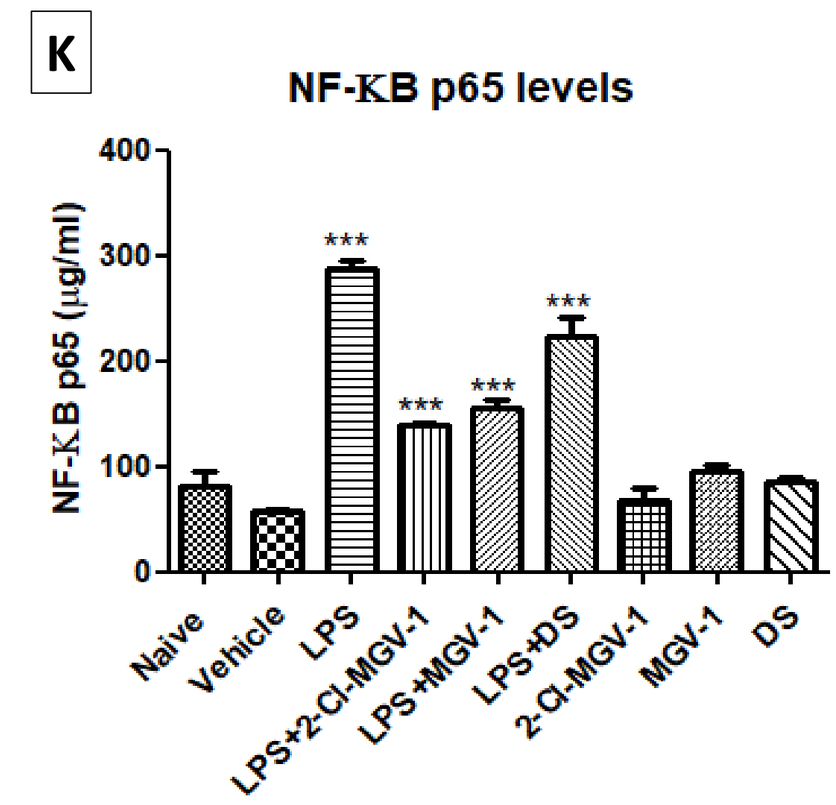


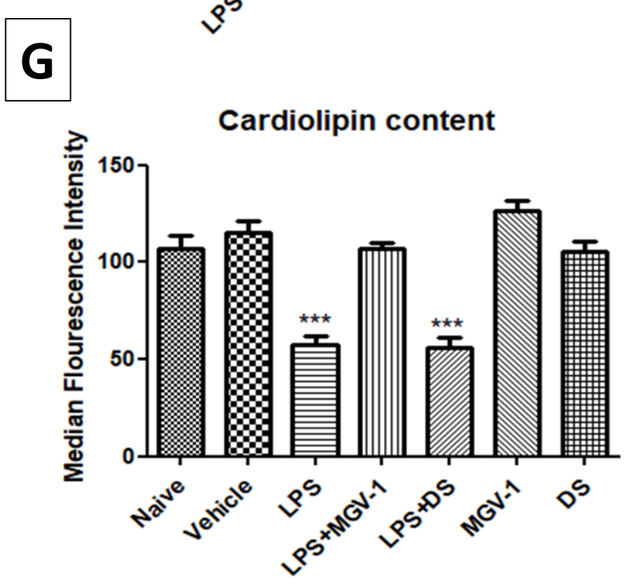


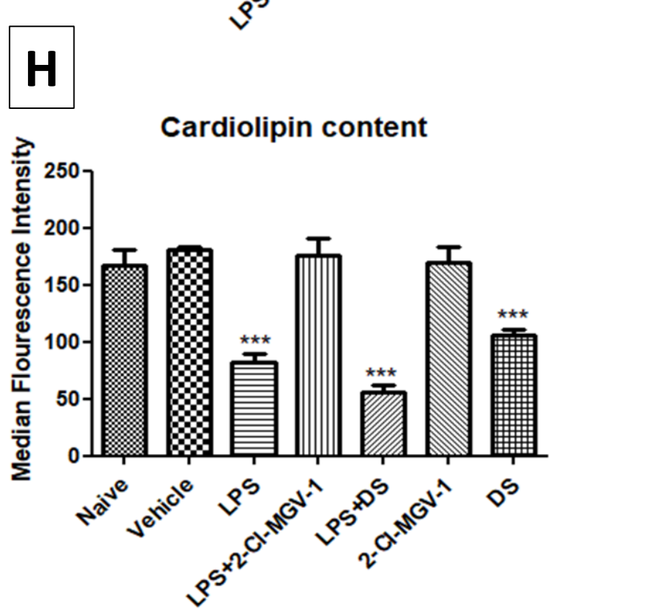


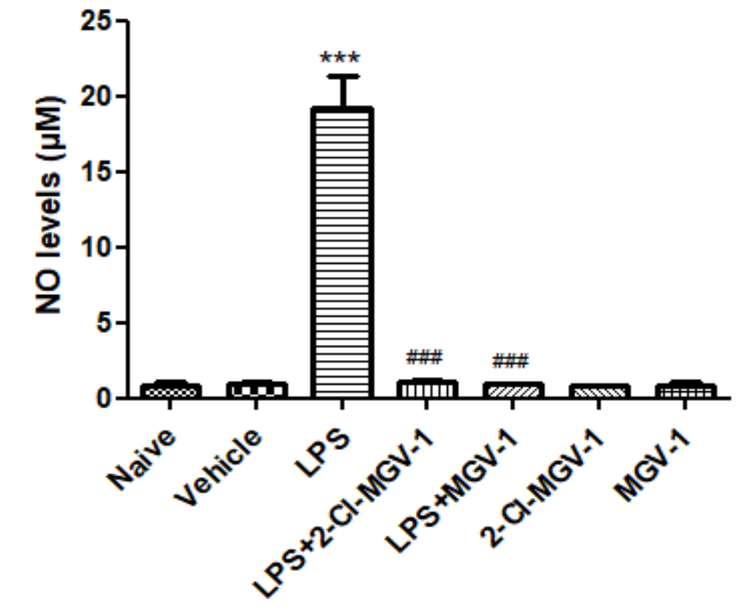


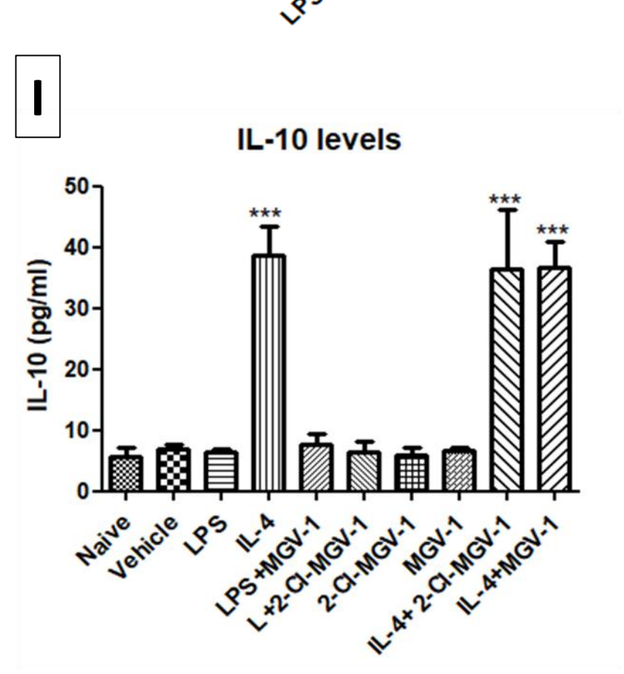


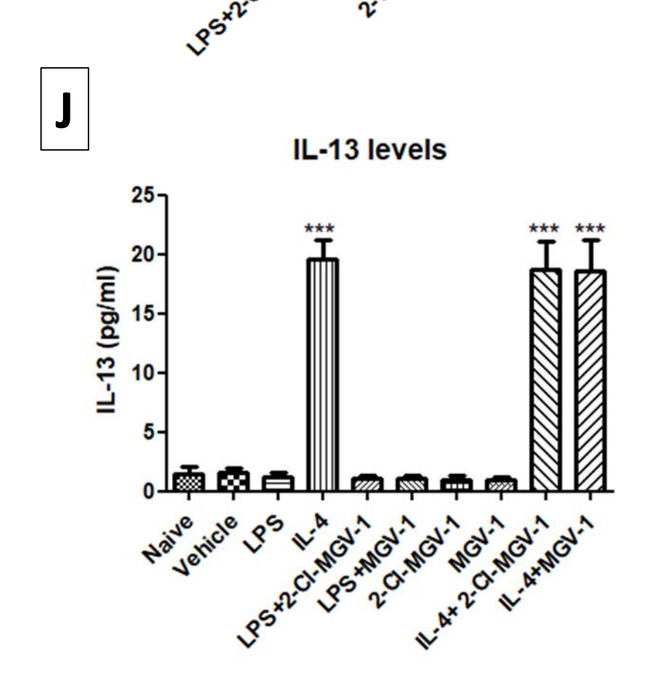


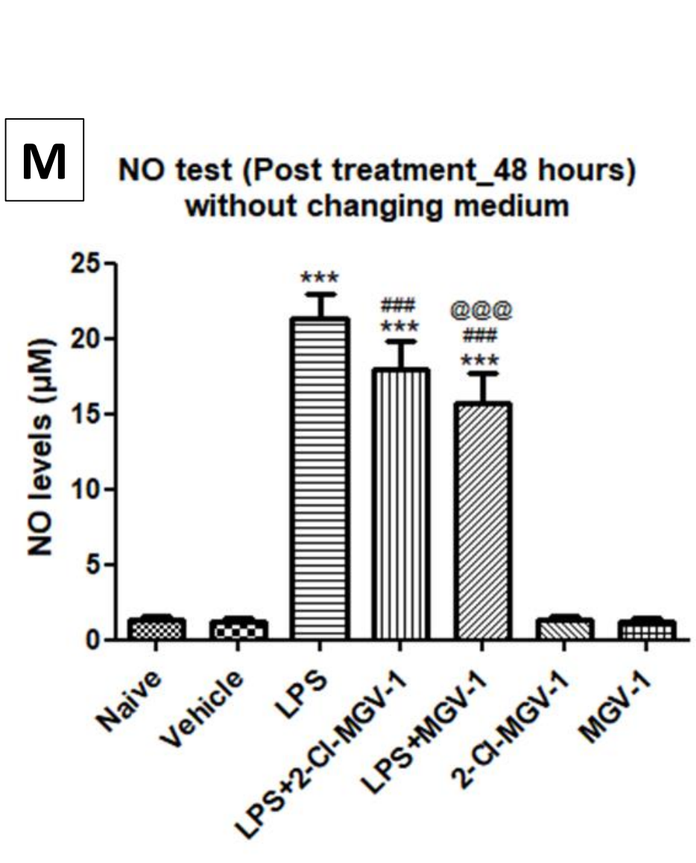












Conclusion

- Our current study shows that the TSPO ligands 2-Cl-MGV-1 and MGV-1 are capable to suppress the inflammatory responses of LPS-induced activated microglia.
- This anti-inflammatory activity may be relevant to the therapy of neuro-inflammatory diseases or disorders associated with neuro-inflammation.
- The reduction caused by 2-Cl-MGV-1 and MGV-1 was similar with no significant differences.

Summary of findings

- **Co-administration of the LPS with TSPO ligands (final concentration- 25 μM) reduce significantly the release of (interleukin) IL-6 from 16.9-fold to 2.5-fold, IL-β from 8.3-fold to 1.6-fold, interferon-γ from 16.0-fold to-2.2 fold, and tumor necrosis factor-α from 16.4-fold to 1.8-fold by blocking NF-κB pathway.**
- **Assessment of initiation of ROS generation and cell metabolism assay show significant protective effects of these two novel TSPO ligands.**
- **No alterations in IL-10 and IL-13 were detected.**