The anti-inflammatory effect of sulforaphane in the brain

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Introduction: Brain inflammation is involved in several neurological pathologies, such as stroke, multiple sclerosis and Alzheimer’s disease1, which continue to have unmet clinical needs. Consequently, research for efficacious anti-inflammatory agents is ongoing. Sulforaphane (SFN), an isothiocynate derived from cruciferous vegetables, has been widely studied in the field of oncology where its beneficial effects have been numerous 2. More recently, SFN’s protective effects following damage to the brain have indicated similar protective effects 3, 4. The effect of SFN on leukocyte-endothelial interactions has yet to be visualised.

Aim: To investigate the ability of sulforaphane (i.p, 5mgkg⁻¹) to protect the cerebral microvasculature against experimental endotoxaemia.

Methods and Results: Intra vital microscopy was used to visualise the cerebral microvasculature. C57Bl6 mice were anaesthetised with Ketamine (150mgkg⁻¹)/Xylazine(7.5mgkg⁻¹), cannulated via the jugular vein and injected with Rhodamine 6G, a fluorescent dye taken up by leukocytes. Preliminary data indicated neither sham surgery nor systemic saline increased leukocyte-endothelial interactions, whereas; LPS (i.p, 4mgkg⁻¹) caused a significant increase in leukocyte-endothelial measured as indicated by increased cell flux (1.4±0.7 cells/min in sham/1.05±0.3 cells/min in saline treated vs. 6.8±1.7 cells/min in LPS treated mice), decreased rolling velocity (431.7±242.6 µm/sec in sham/ 286.1±112.9 µm/sec in saline treated vs. 22.8±2.2 µm/sec in LPS treated mice) and increased numbers of adherent cells (0.1±0.1cells/min/100µm in sham/0.7±0.5 in saline treated vs. 5.2±0.8cells/min/100µm in LPS treated mice). No significant leukocyte-endothelial interaction was observed in arterioles in any mice.

Following this model establishment the effect of systemic prophylactic SFN (4mg/kg) was investigated. SFN significantly reduced cell flux, (6.8 cells/min in LPS treated mice vs. 1.1±0.4 cells/min in SFN/LPS treated mice), increased rolling velocity (22.8 µm/sec in LPS treated mice vs. 79.7±22.6 µm/sec in SFN/LPS treated mice) and decreased cell adhesion (5.2 cells/min/100µm in LPS treated mice vs. 1.7±0.6 cells/min/100µm in SFN/LPS treated mice) in pial venules when compared to mice treated with LPS alone; and significantly reduced cell adhesion (1.7 cells/min/100µm in SFN/LPS treated mice vs. 4.2±0.8 cells/min/100µm in corn oil/LPS treated mice) in SFN/LPS treated mice treated compared with corn oil (SFN vehicle)/LPS treated mice. Statistical analysis was performed using ANOVA and Bonferroni post-hoc test. P<0.05. n= 4 sham surgery mice; n=6 mice in all other groups.

Conclusion: These results indicate that systemic LPS infection induces an inflammatory response within the brain. Furthermore, prophylactic systemic administration of SFN reduces leukocyte-endothelial interactions within the cerebral microvasculature. These novel results suggest SFN as a possible therapeutic strategy in the resolution of inflammation.