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ECTRIMS Online Library. Jörg S. Sep 15, 2016; 146996

Abstract: 141

Type: Oral

Abstract Category: Pathology and pathogenesis of MS - Environmental risk factors

Recently, it was demonstrated that a high-salt diet may aggravate neuroinflammation via the induction of T helper cell (Th) 17 responses. Novel strategies to investigate the systemic sodium exposure revealed that a high-salt load is accompanied by periodical sodium storage in the interstitium of the skin thus rendering this organ a promising compartment to investigate the role of sodium chloride in multiple sclerosis (MS) pathogenesis.

We here investigated the role of cutaneous sodium storage during neuroinflammation in murine myelin oligodendrocyte glycoprotein (MOG) induced experimental autoimmune encephalomyelitis (EAE) as a widely used MS model. Seven Tesla ^{23}Na magnetic resonance spectroscopy (7T ^{23}Na-MRS) revealed a specific sodium enrichment in the skin after induction of active EAE (naïve 24.2 ± 0.8 mM vs EAE 31.6 ± 0.9 mM; n=4, $p< 0.01$). Inductively coupled plasma mass spectrometry of freeze-dried tissue confirmed this specific sodium enrichment in the skin (naive 2.9 ± 0.1 g/kg vs EAE 3.8 ± 0.3 g/kg, n=4, $p< 0.05$) with no difference for skin potassium or sodium concentrations in other organs. This effect was not governed by local inflammation at the immunization site since a similar sodium enrichment was also seen in MOG transgenic 2D2 mice (4.5 ± 0.4 g/kg, n=4). mRNA expression analyses of skin tissue revealed a regulation of salt induced genes and a significant increase of pathogenic Th cell signature genes during neuroinflammation. This finding was corroborated by flow cytometry analysis of dermal tissue on day 16 of EAE with significantly higher Th1 and Th17 cell frequencies as compared to naïve control mice (n=8, $p< 0.001$). Moreover, a T cell transfer experiment demonstrated a selective enrichment of MOG activated T cells in the skin with higher frequencies of CD44+/CD25+ cells as compared to the blood and spleen (n=5, $p< 0.001$). As a therapeutic modulation, the administration of the loop diuretic furosemide significantly reduced the sodium concentration in the skin (7T ^{23}Na-MRS; control 31.3 ± 0.6 mM vs furosemide 27.7 ± 0.4 mM; n=10, $p< 0.0001$) thereby ameliorating the early course of EAE (n=10 per group, $p< 0.05$).

Our data highlight a role for the skin as an important regulator of sodium homeostasis in neuroinflammation thus identifying a new compartment linking diet and MS pathogenesis.

Disclosure: RG and RAL received research support or personal compensation for activities

with Bayer, Biogen, Genzyme, Merck, Novartis, Roche and TEVA Pharma. There are no disclosures directly related to this study.

All other authors: nothing to disclose