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OC-023 - (23752) - BLOOD SPINAL CORD BARRIER COMPROMISE IN SPINAL MUSCULAR ATROPHY PATIENTS

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Spinal muscular atrophy (SMA) is a paediatric motor neuron disease, that if left untreated, is commonly fatal in early childhood. Beyond characteristic motor neuron loss and skeletal muscle atrophy, patients display significant endothelial cell dysfunction resulting in gross vascular bed abnormalities. Specifically, our previous work demonstrated microvascular defects in the SMA spinal cord that could trigger or exacerbate neurodegeneration.

Here, we extend that study by evaluating the morphology and integrity of the blood–spinal cord barrier (BSCB) and quantifying the contribution of CNS glia to SMA pathology. Human post-mortem spinal cord samples were obtained from tissue banks (Johns Hopkins University, NIH-Neurobiobank and BRAIN-UK). Transmission electron microscopy was used to assess the ultrastructural integrity of BSCB components and immunohistochemistry to detect extravasation of plasma proteins as indicators of barrier disruption. Microglia were characterized using Iba1 and CD68 markers to determine their activation state.

Damage of all BSCB layers was observed in SMA, with endothelial cells, pericytes and astrocyte end-feet exhibiting swelling, vacuolization and membrane rupture. The presence of extravascular fibrinogen and haemoglobin confirmed BSCB compromise. Ninety-eight percent of microglia displayed an activated phenotype, indicative of a strong neuroinflammatory response.

The ingress of toxic blood proteins into the CNS can drive neuronal pathology, therefore these findings implicate BSCB breakdown as a potential contributor to motor neuron loss in SMA. Current therapies were developed to rescue motor

neurons and may not target cells of the BSCB. Future treatment strategies must incorporate novel approaches to more comprehensively manage SMA and improve long-term patient outcomes.

Palavras-chave : Neurodegeneration, Blood spinal cord barrier, Endothelial cells