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NanoString analysis of neuroinflammation in multiple system atrophy

Introduction: Multiple system atrophy (MSA) is an adult-onset neurodegenerative disease characterised by aggregation of α -synuclein in oligodendrocytes to form glial cytoplasmic inclusions (GCIs). We have previously demonstrated that microglial activation occurs in both severely affected regions of MSA brain and regions mildly affected, with few GCIs. Showing that both pro-inflammatory (CD68 positive) and anti-inflammatory (Arginase-1 positive) microglia are present in both MSA and control brain. To obtain a more detailed view of the complex inflammatory environment of MSA, we investigated the gene expression profiles of 256 inflammatory genes in post-mortem MSA brains.

Materials and Methods:

Patient brain donation enabled detailed post-mortem neuropathological examination and confirmed diagnosis of mixed MSA or control brain. Whole tissue was isolated from frontal cortex and cerebellar white matter of control (n=?) and MSA cases (N=6) and homogenised, total RNA was extracted using the Qiagen RNeasy kit and quality checked using an Eppendorf spectrophotometer. NanoString nCounter technology was used to analyse the levels of RNA associated with inflammation. Data analysis was performed using NanoString nSolver software.

Results:

Analysis of NanoString data has revealed a series of genes (n=286) which have significantly altered levels in MSA frontal cortex compared to control. Of particular note in the current study, three proinflammatory genes were upregulated while anti-inflammatory genes were downregulated in MSA compared to control.

Conclusion:

Our work confirms that neuroinflammation is a feature of MSA and may be important in disease pathogenesis. Further investigations into the individual gene targets and their mechanisms of action in MSA pathogenesis are needed to identify their influence on the underlying

disease mechanisms. These findings improve our understanding of this rare disease and may point to potential treatment strategies for MSA.